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N. H. Perry MD

June 1906

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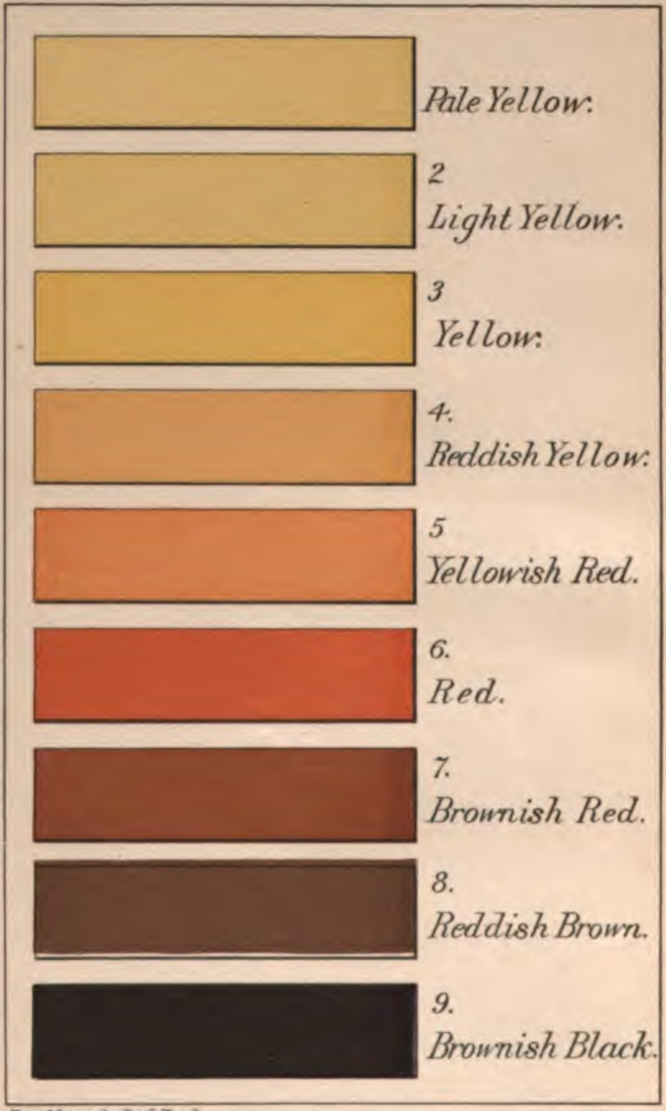


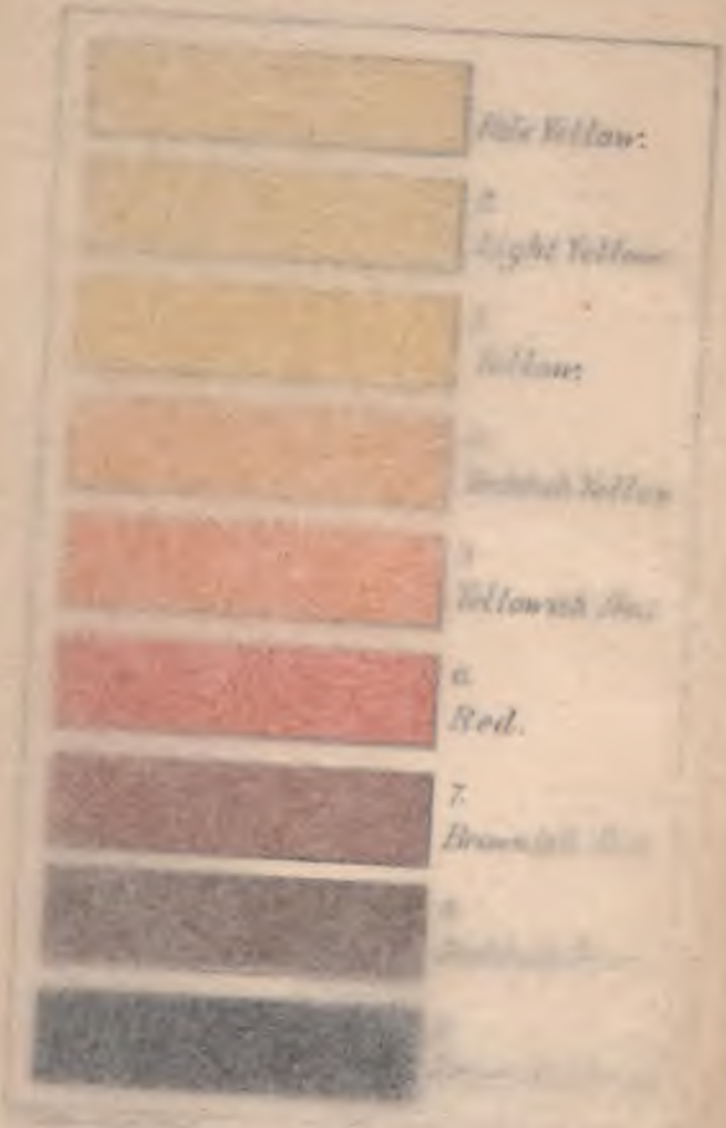
From Nature by Dr. J. Vogel.

VOGEL'S SCALE OF URINE TINTS

URANALYSIS

DIAGNOSIS

PLATE I.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PRACTICAL URANALYSIS
AND
URINARY DIAGNOSIS.

A Manual for the Use of Physicians, Surgeons, and Students.

BY

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WITH NUMEROUS ILLUSTRATIONS, INCLUDING PHOTO-ENGRAVINGS AND COLORED PLATES.

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J53
P98
1895.

TO THE
PROFESSORS, PAST AND PRESENT;
TO THE
FELLOWS, ALUMNI, AND STUDENTS,
OF MY
ALMA MATER,
THE FOLLOWING PAGES ARE
AFFECTIONATELY INSCRIBED
BY
THE AUTHOR.

24708

PREFACE.

Our present knowledge of the urine and of diseases of the urinary organs may be said to be altogether abreast with other departments of scientific and practical medicine. At present, however, this knowledge is only accessible to the student through somewhat extended search through general works on Medicine, Surgery, Pathology, Physiological Chemistry, Microscopy, etc., in addition to the various works devoted to this special subject. European writers,—especially those in our language,—following the sharp division between medical and surgical diseases, have invariably considered the present subject, both in general and special works, either from an exclusively medical or surgical point of view, and American writers thus far, without exception, have followed this example. But in America the whole profession is taught and qualified to practice both medicine and surgery, and, therefore, the above-mentioned custom compels the student, in order to gain a complete knowledge of this subject, to study several authorities, entailing increased expense and time, if not, indeed, confusion. Believing, therefore, that American authors should, so far as is possible, deal with the whole subject comprised in the titles of special works, it has been the aim of the author in the present work to furnish the student, physician, and surgeon, in one moderate-sized volume, the essential features of our knowledge of the urine and urinary diagnosis, thoroughly up to date, and in the most systematic, practical, and concise form. In carrying out this object an effort has first been made to bring out prominently the relations of the chemistry of the urine to physiological processes and pathological facts. Thus, in dealing with normal urine, each constituent has been considered, so far as at present is known, in the following order: Its chemical nature and composition; its source in the economy; the significance of its increase or decrease in the urine, with the relations of these to metabolic processes, food-supply, physical surroundings, and tendency toward disease; and, finally, the most approved methods of its detection and determination have been described. In dealing with abnormal urine each morbid constituent has been considered, so far as at present is known, in the following order: Its chemical nature and composition; its source in the economy; the clinical significance of its appearance in the urine; and, lastly, the most approved methods of its detection and determination have been described. This method aims at teaching not only how to detect, isolate, and determine the constituents of the urine, normal and abnormal, but also to determine the presence of disturbed physiological processes, to detect the presence of pathological changes, and to measure the degree of both.

The second division of the work—Urinary Diagnosis—aims at a concise description of the special features of the urine that indicate the presence of special pathological processes in progress in the economy, whether they be local or general, medical or surgical, together with a brief enumeration of the leading clinical symptoms of each disease, and, in most cases, an epitome of their nature and etiology.

Having compassed the whole text, it is designed that the investigator will next be in a position to utilize the information thereby furnished to the best practical diagnostic purposes, and give him the mastery over the diseases considered,—*for, as a rule, he who has accurately diagnosticated disease, has already constituted himself its conqueror.*

The author has freely quoted the views of standard authorities, endeavoring in all cases to make due acknowledgment of the same throughout the text. Should, however, any of the latter have been overlooked, he desires here to express his obligations for all knowledge derived from fellow-laborers in the same field of work.

Some repetitions of matter will be noted, both in the text and foot-notes, the object being to save references to other parts of the work and render it more convenient as an open hand-book for the laboratory table.

Over twenty-five years' experience, coupled with a somewhat liberal examination of the literature of this subject, as well as considerable practical observation and experiment, have enabled the author to contribute some original matter and methods, which, he trusts, will prove to be an advance in certain practical departments of the subject.

Finally, an appendix has been added upon the subject of urinary examinations for life-insurance. Believing, from some experience as a medical director, that on the one hand life-insurance associations are often unjustly called upon to pay insurance on uninsurable lives, and on the other hand that applicants are often deprived of the privileges of life-insurance to which they are justly entitled, especial pains have been taken with this department of the work, with the earnest hope of contributing, in some degree, to the amelioration of these two forms of injustice.

57 East Twentieth Street,
Chicago, September, 1894.

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PART I.

ANALYSIS OF URINE.

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ABNORMAL URINE. PROTEIDS.
CARBOHYDRATES.
URINARY SEDIMENTS.
CHEMICAL SEDIMENTS.
ANATOMICAL SEDIMENTS.
GRAVEL AND CALCULUS.

SECTION I.

GENERAL CONSIDERATIONS.

THE recent advances in our knowledge of physiological chemistry, with the more extended and refined use of the microscope, have lent great precision to the study of the composition of the urine, and thereby furnished us with a keener insight into the relationship of the urine to the organism, both in health and in disease. The variations in nutrition and waste are accurately recorded in the urine hour by hour, and by an intelligent interpretation of modern methods of uranalysis these physiological tides may now be read as accurately as we can number the pulsations of the heart. By the same methods we are now enabled to measure the hourly inroads upon the organism made by disease with a precision often greater than is afforded by the pulse or the clinical thermometer. Wherever in the economy pathogenic processes seriously disturb nutrition or normal metabolism, the results are recorded in the urine, because the urine, more eminently than any other excretion, represents the equation of these changes.

The accurate study of the urine, therefore, has become one of the essential features in advanced clinical medicine. Indeed, through uranalysis alone can an almost daily increasing number of diseases be determined, their intensity be gauged, and their progress toward recovery, or their tendency toward a fatal termination, be predicted. While it is impossible to diagnosticate all diseases from the urine, it is, nevertheless, true that no serious disease can be in progress in the economy without giving rise to more or less marked changes in the character of the urine, and therefore we can no longer afford to exclude urinary analysis from the scientific investigation of any serious form of disease.

In order to fully comprehend the relations of the urine to the organism under the influence of the various pathological conditions, it is first necessary to become acquainted with the physiology of secretion and excretion of the urine, as well as the normal composition of the latter, together with those fluctuations which are included within the range of health.

While a number of points in the physiology of the secretion and excretion of the urine still remain undetermined, it may be stated that our present knowledge of the subject indicates that the process is partly a physical and partly a vital one. The older theory of Bowman, based on the anatomical construction of the kidneys, taught that the epithelial cells of the urinary tubules constitute the true secretory structure of the kidneys, while the glomeruli act as mere filters for the escape of the watery elements from the blood. According to Bowman, therefore, the filtrate from the glomeruli consists almost solely of water, which aids in extracting the other constituents of the urine from the epithelium of the tubules in its passage along the latter.

Ludwig, on the other hand, explains the process on purely physical grounds, basing his theory on the varying degrees of blood-pressure in the glomerular circulation and the interchange of constituents by diffusion or osmosis in the urinary tubules. Assuming that the relative blood-pressure in the kidney is greatest in the glomerular tufts in consequence of the resistance to the efferent circulation, Ludwig holds that, consequently, a free exudation of water takes place from the tufts, with, perhaps, some dissolved salts. This renders the blood much concentrated —thickened—when it reaches the capillary plexus surrounding the convoluted tubes, while within the latter is now the thin, aqueous filtrate from the tufts. It will be noted that such conditions form all the essential elements for active osmosis,—within the tubules thin, watery fluid, and in the surrounding capillaries thickened blood, while between them is interposed a thin membrane,—the tubular wall. An interchange of elements consequently occurs, by means of which water from the urinary tubules passes into the blood; while, on the other hand, the products of retrograde tissue changes—urea and salts—pass from the blood into the tubules, mingling there with the thin fluid and constituting the urine.

Unfortunately for the theory of Ludwig, he leaves out of consideration any function on the part of the renal epithelium, which violates analogical reasoning, because the renal epithelium possesses the anatomical peculiarities of glandular epithelium, the function of which is secretory or selective wherever else met with throughout the economy. Moreover, both clinical and pathological experiences teach that the renal epithelium possesses a distinct and important function in the elaborating processes of the kidney; for, in diseases which destroy or remove this epithelium from the urinary tubules, urea and allied products are retained in the system, and the phenomena of uræmia is evoked. Finally, the interesting experiments of Heidenhain have conclusively proved that the renal epithelium possesses a distinct selective power, as follows: If a slightly-concentrated solution of indigo-sulphate of sodium be injected into the blood of an animal, a blue color will soon after be communicated to the urine and the epithelium of the convoluted tubules and ascending limbs of Henle's tubes, while the Malpighian structures do not present the slightest trace of blue. If the spinal cord of an animal be first divided and the indigo injection be subsequently made, the following phenomena may be observed: No urine whatever reaches the bladder, but the blue color passes into the kidney and may be seen in the convoluted tubes and ascending limbs of Henle's tubes as before. Ten minutes after the injection the coloring matter is found solely in the epithelial cells in the locations above noted. An hour after the injection the epithelial cells are found colorless, the blue matter having passed into the lumens of the tubes, where, in the absence of water from the glomeruli, it concentrates into crystals. This establishes a distinct eliminative power on the part of the renal epithelium altogether independent of the glomeruli, because the latter were paralyzed by section of the spinal cord.

It seems altogether likely, therefore, that the chief specific principles of the urine are eliminated by the renal epithelium, precisely as are the coloring matters in Heidenhain's experiments. This seems the more probable now, since it is pretty well established that the chief urinary constituents—urea, uric acid, etc.—exist preformed in the blood. Our present knowledge on this subject warrants the conclusion that the production of the urine is chiefly an elaborating or secreting process, regulated in its fluidity by the glomerular system. In other words, that the water and some of the salts are secreted by the glomeruli, the peculiar anatomical construction of which permits a varying degree of activity corresponding chiefly with the varying degrees of blood-pressure and blood-fluidity; while, in the main, the solid excretory products of the urine are eliminated by the epithelium of the renal tubules, through their vital, selective, or secretory power, as in all other glandular structures of similar anatomical construction.

Composition of the Urine.—The constituents of normal urine are derived from the elements of retrograde tissue metamorphosis in the healthy state of the organism, together with certain waste products of substances introduced into the system in the form of food and beverages. The normal constituents of the urine, according to the basis of classification adopted by Hoppe-Seyler, are as follow: 1. Urea and related substances,—uric acid, allantoin, oxalic acid, xanthin, guanin, creatinin, thio- (sulpho-) cyanic acid. 2. Fatty and other non-nitrogenous substances,—fatty acids of the series $C_nH_{2n}O_2$; oxalic, lactic, glycero-phosphoric acids; very small quantities of certain carbohydrates—sugar (Brucke). 3. Aromatic substances,—the ethereal sulphates of phenol, cresol, pyrocatechin, indoxyl, and skatoxyl; hippuric

AMOUNTS OF URINARY CONSTITUENTS PASSED IN TWENTY-FOUR HOURS.

CONSTITUENTS.	WEIGHT, 66 KILOGRAMMES.	PER KILOGRAMME OF BODY-WEIGHT.
Water	1500.00 grammes.	23.000 grammes.
Total solids	72.00 "	1.100 "
Urea	33.18 "	0.500 "
Uric acid	0.55 "	0.008 "
Hippuric acid	0.40 "	0.006 "
Creatinin	0.91 "	0.014 "
Pigment and other organic matters	10.00 "	0.151 "
Sulphuric acid	2.01 "	0.030 "
Phosphoric acid	3.16 "	0.048 "
Chlorine	7–8.00 "	0.126 "
Ammonium	0.77 "	
Potassium	2.50 "	
Sodium	11.09 "	
Calcium	0.26 "	
Magnesium	0.21 "	

acid, aromatic oxyacids. 4. Other organic substances,—pigments; ferments, especially pepsin; mucus, and humous substances. 5. Inorganic salts,—chlorides of sodium and potassium, potassium sulphate; sodium, calcium, and magnesium phosphates; silic acid, ammonium compounds, and calcium carbonate. 6. Gases,—nitrogen and carbonic acid.

The quantitative composition of the human urine is best expressed in the classical table of Parkes, as on preceding page.

The proportion between the solids of the urine and the water, according to Becquerel, is as follows: Water 967 grains, solids 33 grains in each 1000 grains. Of the solid matters the organic elements amount to about 24.865 grains, while the inorganic constituents are about 8.135 grains in each 1000 grains.

Changes in the Urine upon Standing.—Considering the somewhat complex composition of the urine, holding as it does in solution both organic and inorganic compounds which are subject to organic as well as chemical alterations, as might be expected, the urine is subject to more or less rapid changes after it has been voided. The rapidity of these changes depends chiefly upon the reaction and concentration of the urine, the temperature of the room in which it is kept, and the degree of access to micro-organisms. A normal acid urine usually first precipitates the amorphous urates, then uric acid, and frequently oxalate of calcium. Under ordinary circumstances these changes take place within three days after the urine is voided. At ordinary temperatures (70° to 74° F.—21.1° to 23.3° C.), after twenty-four to forty-eight hours' standing, and much sooner under high temperatures (say, 100° F.—37.8° C.), the urine begins to become dull and opaque from the presence of micro-organisms,—*fission fungi*. These multiply, and at the end of four or five days, as a consequence, ammoniacal decomposition sets in; that is to say, through the activity of the fungi the urea is gradually transformed into carbonate of ammonium. The urine becomes more and more alkaline from the liberation of ammonium carbonate. The amorphous urate deposit now becomes transformed into urate of ammonium, uric-acid crystals are substituted by characteristic prismatic crystals of ammonio-magnesian phosphate (triple phosphate), and amorphous granules of calcium phosphate are deposited in quantity at the bottom and sides of the vessel. Finally, the bacterial activity diminishes as the urine becomes strongly alkaline, and the micro-organisms ultimately perish. Urines of low density and feeble acidity undergo the above-described changes more rapidly, and, moreover, as a rule, do not deposit urates.

A change sometimes occurs in acid urine, consisting of progressive acidity, in which the urine darkens in color and deposits uric acid and urates and sometimes calcium-oxalate crystals, with the frequent presence of yeast-fungus and bacteria. This was formerly termed the "*acid fermentation*," but, according to Scherer, it is caused by the mucus, which acts as an enzyme, or ferment, producing an acetic-acid or lactic-acid fermentation, with precipitation of uric acid and acid urates.

Collection of Urine for Analysis.—For the purpose of quantitative determination of the urinary constituents it is essential to have a sample of a mixture of the whole product of the kidneys for twenty-four hours. The varying degrees of solid and fluid contents of the urine at different hours of the day render the observance of the above rule strictly essential if we desire a sample of urine that will represent the average product of the kidneys. In order to guard against the early changes in the urine which have just been described, the urine should be collected in a *perfectly-clean* vessel,—preferably a half-gallon bottle,—which should stand in a cool but dry room during the collection, and the bottle should be corked after each addition of urine.

For qualitative determination of the *morbid* products of the urine—as sugar, albumin, etc.—it is preferable to collect a freshly-voided sample of the urine about three hours after a meal, *not the urine voided in the morning on rising.* Of all urines, that voided in the morning on rising is the least likely to contain albumin or sugar. When these substances are only occasionally present in the urine, they are most likely to be found after food and exercise. Finally, in collecting a sample of urine for purely microscopical examination, it should be perfectly fresh and as concentrated as possible. It has been shown that the urine soon undergoes ammoniacal changes upon standing, the result of which is to render it more or less strongly alkaline. Now, morphological elements, as epithelium and casts, are soluble in alkaline solutions; so that they may, if present when the urine is voided, become unrecognizably altered, or even disappear, if the foregoing precautions be not observed. Concentration of the urine may be obtained by directing the patient to abstain, as much as consistent with comfort, from the use of fluids for twenty-four hours.

PHYSICAL CHARACTERS OF THE URINE.

Color.—The average color of normal urine of specific gravity 1020 and 1500 cubic centimetres' volume for twenty-four hours is straw or wine yellow,—amber-colored. This, however, is subject to considerable variations at different times of the day, and under varying circumstances included within the range of perfect health. Thus, from an almost colorless (watery) appearance the urine may range through the yellows and reach reddish brown. The pale, watery urine in health contains *relatively* small amounts of coloring matter, as well as urea and salts. It is seldom very acid, often neutral or feebly alkaline, and it is most often brought about by copious drinking. Highly-colored urine, on the contrary, is usually concentrated, containing *relatively* large quantities of solids and coloring matters. Its specific gravity is high, and its reaction is usually sharply acid. It results from diminished excretion of water by the kidneys, while the solids and coloring matters are normal or increased. In health it may occur after hearty meals, vigorous exercise, or when the skin has been unduly active and little fluids imbibed.

Pathologically the urine is subject to much wider variations in color than in health. This may be due either to increase or diminution of the normal coloring matters, on the one hand, or, on the other, to the addition of abnormal pigments. Abnormally light-colored urine is often due to polyuria, as in diabetes, hysteria, and convulsions; or it is often observed in diseases of the kidney which not only increase the normal amount of water in the urine, but which also reduce the solids and coloring matters,—notably, interstitial nephritis and amyloid degeneration of the kidneys. Highly-colored urine, approaching red, is most often induced by acute pyrexia and inflammations. This is due in part to concentration of the urine, though largely also to the presence of uro-erythrine. The distinctly red tints of the urine are always due to the presence of foreign coloring matters, most often blood. The dark-brown tints may be due to the presence of methæmoglobin in diseases of the kidney attended by hæmorrhage. The urine in cases of melanotic cancer sometimes becomes almost black, especially after standing for some time. Green urine, of dull hue, is common in jaundice, the color being due to the presence of biliverdin. The urine is frequently of a greenish hue in diabetes, notably when the urine contains a high percentage of sugar. Blue urine, of dull tint, is not uncommon in cholera and typhus, owing to the presence of indigo. Finally, certain drugs, when swallowed, affect the color of the urine to a more or less marked degree: thus, rhubarb and senna cause brown or reddish tints; carbolic acid sometimes causes a black color in the urine, notably after the urine has stood some time; the same results follow the ingestion of naphthalin, hydrochinon, resorcin, and pyrocatechin. Lastly, santonin, when swallowed, always causes a yellow color in the urine, of decided hue.

J. Vogel has, at considerable labor, constructed a scale of colors of the urine from nature, which has, in a manner, become standard for comparative purposes. These colors he expresses as (1) pale yellow, (2) light yellow, (3) yellow, (4) reddish yellow, (5) yellowish red, (6) red, (7) brownish red, (8) reddish brown, and (9) brownish black. (See Frontispiece.) He divides these into three groups, the first three being yellow urines, the second three reddish urines, and the last three brown or dark urines. In comparing the color of the urine with the scale the urine should first be filtered if not perfectly clear, and it should

I	II	III	IV	V	VI	VII	VIII	IX	
1	2	4	8	16	32	64	128	256	Pale yellow.......= I
	1	2	4	8	16	32	64	128	Light yellow......= II
		1	2	4	8	16	32	64	Yellow ....= III
			1	2	4	8	16	32	Reddish yellow ...= IV
				1	2	4	8	16	Yellowish red.....= V
					1	2	4	8	Red ....= VI
						1	2	4	Brownish red .....= VII
							1	2	Reddish brown....= VIII
								1	Brownish black...= IX

be examined by transmitted light in a glass vessel at least three or four inches in diameter. It is claimed that the shades of color in Vogel's scale correspond to certain relative amounts of coloring matter in the urine, and the test-table on preceding page has been constructed for the purpose of color analysis.

Application.—The table indicates how much coloring matter equal parts of urine of different colors contain relatively. Thus, if a certain volume of pale-yellow urine contain 1 part of coloring matter, the same volume of yellowish red contains 16 parts; of red, 32 parts; of brownish black, 256 parts. It further indicates that 1 volume of yellow urine contains as much coloring matter as 4 volumes of reddish yellow, or 32 volumes of pale yellow, etc. If, therefore, one person pass 1000 cubic centimetres of yellow urine in twenty-four hours, and another 4000 cubic centimetres of pale-yellow urine in the same time, both secrete an equal amount of coloring matter. In order to make an approximate comparison by figures, Vogel places the quantity of coloring matter which 1000 cubic centimetres of pale-yellow urine contain = 1.

Example.—1800 cubic centimetres of urine of yellow color are passed. 1000 cubic centimetres of pale-yellow urine equal one part of coloring matter.

But yellow, according to the table, contains four times as much; therefore the following proportions: $1000:4=1800:x$ $=7.2$ as the amount of coloring matter in 1800 cubic centimetres of yellow urine, the coloring matter in 1000 cubic centimetres of pale-yellow urine being considered as the unit.

Halliburton gives the following concise table of color variations of the urine, with their causes. (See next page.)

Odor.—The odor of normal freshly-voided urine is peculiar,—of slightly aromatic nature,—due, it is believed, to phenylic, taurylic, damoluric, and damolic acids in minute quantities. There is considerable difference in the intensity of the uric odor in health, always being most pronounced in concentrated urine. If the urine become alkaline from standing, it acquires a peculiar, repulsive, putrescent odor, in which ammonium is plainly distinguishable. The former is due to the decomposition of mucus and other organic matters, while the ammonium is in the

COLOR.	CAUSE OF COLORATION.	PATHOLOGICAL CONDITION.
Nearly colorless.	Dilution, or diminution of normal pigments.	Nervous conditions: hydruria, diabetes insipidus, granular kidney.
Dark yellow to brown-red.	Increase of normal, or occurrence of pathological, pigments.	Acute febrile diseases.
Milky.	Fat-globules.	Chyluria.
	Pus-corpuscles.	Purulent diseases of the urinary tract.
Orange.	Excreted drugs.	Santonin, chrysophanic acid.
Red or reddish.	Unchanged hæmoglobin.	Hæmorrhages, or hæmoglobinuria.
	Pigments in food (logwood, madda, bilberries, fuchsin).	
Brown to brown-black.	Hæmatin.	Small hæmorrhages.
	Methæmoglobin.	Methæmoglobinuria.
	Melanin.	Melanotic sarcoma.
	Hydrochinon and catechol.	Carbolic-acid poisoning.
Greenish yellow, greenish brown, approaching black.	Bile-pigments.	Jaundice.
Dirty green or blue.	A dark-blue scum on surface, with a blue deposit, due to an excess of indigo-forming substances.	Cholera, typhus; seen especially when the urine is putrefying.
Brown-yellow to red-brown, becoming blood-red upon adding alkalies.	Substances which are introduced into the system with senna, rhubarb, and chelidonium.	

form of carbonate, resulting from bacterial decomposition of a part of the contained urea,—$CON_2H_4 + 2H_2O = (NH_4)2CO_3$.

Certain substances, when ingested, impart to the urine peculiar and unnatural odors. Thus, a characteristic odor is acquired after eating asparagus, and an odor not unlike violets is produced by the administration of turpentine-oil. The odor of cubebs, copaiba, sandalwood-oil, garlic, tolu, etc., are more or less communicated to the urine when taken internally. These odors may be serviceable by indicating that the patient has taken certain medicines or foods. Beauvis and others have claimed that the peculiar odors after asparagus and turpentine-oil do not appear in the urine in organic diseases of the kidney. This, if true, might be valuable for diagnostic purposes, but more extended observation has not confirmed the assertion.

Pathologically the odor of the urine renders some information. Thus, if the urine be ammoniacal when voided, it is strong evidence of the existence of cystitis. In suppurating conditions of the upper urinary tract the urine is often peculiarly offensive (putrid), in consequence of its contained decomposing pus, blood, and organic elements. In diabetes the urine often has the odor of acetone. Urine containing cystin possesses an odor, at first, like sweet briar, but subsequently becomes very offensive.

Transparency.—The normal freshly-voided urine may be said to be always macroscopically clear; after standing, a mucous cloud, more or less pronounced, usually appears, which is unchanged by alkalies, heat, or mineral acids. Pathologically the urine may become cloudy from various causes, as the precipitation of urates, carbonates, phosphates, or organic products, as blood, chyle, excess of mucus, pus, bacteria, etc. If the cloudiness of the urine disappear upon the application of gentle heat, it may be concluded that the turbidity was due to the presence of precipitated urates. If, on the contrary, the turbidity increase upon the application of heat, it is due either to precipitation of the earthy phosphates or to albuminous cell-elements, as pus or blood. If the phosphates be the cause of the cloudiness, the latter rapidly clears up by the addition of an acid. If, on the other hand, it become more turbid upon the addition of the acid, it may be concluded that pus, blood, or albuminous cell-elements are the cause of the opacity. If the urine remain unchanged by the acetic acid, or if the turbidity be very slightly increased thereby, it may be concluded that mucus or micro-organisms are the cause of the turbidity.

Consistence.—Normal urine is always of aqueous consistence; that is to say, it drops and flows as does water. Pathologically the urine may become thick and viscid, so that it flows from the vessel slowly and with difficulty, not separating into drops. Such is usually the case when the urine contains a large amount of mucus or pus, and especially if, in addition, the urine be alkaline. Diabetic urine, if heavily laden with sugar, is of diminished consistence, as is evidenced by its tendency to froth when agitated; and the same may be said of highly-albuminous urine. In chylous urine, owing to the contained molecular fat, the fluid often becomes much thickened. In fibrinuria the urine, after standing, sometimes becomes thickened into a jelly-like consistence, so that it may stick to the vessel when the latter is inverted.

Specific Gravity.—The average specific gravity of normal urine of 1500 cubic centimetres (50 ounces) in volume for twenty-four hours is about 1020. Slight variations from this standard are consistent with perfect health, and depend chiefly upon the character of the food taken, as well as the quantity thereof, and the rapidity of tissue metamorphosis. If the diet consist largely of nitrogenous foods, they furnish a higher relative amount of solids than fluids to be excreted by the kidneys, and, consequently, the specific gravity of the urine will be somewhat increased. Upon active muscular exertion oxidation and tissue waste is hastened, which also tends to raise the specific gravity of the urine through furnishing a relatively large amount of solids to be excreted. Copious diaphoresis may bring about a concentrated condition of the urine, with an accompanying increase of specific gravity. The specific gravity of the urine may be lowered by fasting, or by imbibing large quantities of fluids. Very marked departures from the normal specific gravity of the urine often constitute pathological factors of great importance. In nearly all forms of organic albuminuria (Bright's disease) the tendency is toward a lowered specific gravity of the urine.

Acute diffuse nephritis and cyanotic induration of the kidney are exceptions to the foregoing rule; in both these exceptions the increased specific gravity is due to marked diminution of the volume,—concentration. A lowered specific gravity of the urine, especially if the volume of the urine remain normal, should always be regarded as suspicious of renal defect. An important fact to be noted in this connection is that, in most cases of so-called *functional albuminuria*, the specific gravity of the urine is above the normal standard. Prognostically, in cases of nephritis, a reduction of the specific gravity of the urine without alteration of the volume thereof should always be regarded as of serious import. It usually indicates inability of the kidneys to excrete the normal amount of solids, and thus gives warning of approaching uræmia. If the specific gravity of the urine be markedly increased, it is strongly indicative of melituria. Should it reach as high as 1030, or above, search should always be made for sugar.

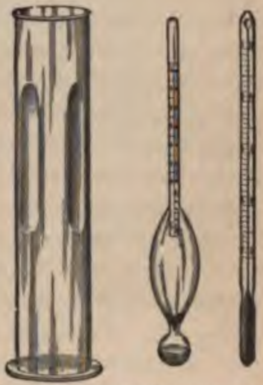

FIG. 1.—SQUIBB'S URINOMETER.

To determine the specific gravity of the urine with accuracy the Mohr-Westphal balance, or pyknometer, is the most trustworthy instrument. A more simple instrument, better suited for general practical use, is one constructed on the principle of an hydrometer, termed the urinometer. If carefully constructed and properly corrected, such an instrument will answer all practical purposes. Unfortunately, however, of all the simple instruments offered for sale the urinometer is the most useless in consequence of its faulty correction, it being not at all uncommon to find them at fault from 3 or 4 to 10 degrees. The urinometers made by E. R. Squibb are recommended as a notable exception to the above rule, as they meet all the requirements of the best instruments. These urinometers are standardized at 25° C. (77° F.), the ordinary temperature of dwelling-rooms, and therefore temperature corrections are usually unnecessary in taking observations. The receiving-jar for the urine is fluted sharply in the middle, preventing the instrument from clinging to the sides; and this is still further secured by the spindle-shaped form of the bulb of the instrument, so that a single point of contact is obtained between the instrument and the jar. Each instrument is carefully tested, and any variation of the scale from the correct standard is marked on the case.[1] A thermometer is furnished, for the purpose of temperature corrections, with each instrument. In taking the specific gravity of the urine with the urinometer the glass-cylinder tube is filled about three-fourths full of the urine, and any froth appearing at the top is removed by filtering-paper or a pipette. The urinometer is next introduced into the urine and touched gently with the finger-tip, so that it sinks and rises a few seconds until it finds the correct level. When it comes to a rest the scale is read on a level with the eye, and the figure on a level with the surface of the urine is marked.

The temperature of the urine immediately after being voided ranges from 85° to 95° F. (29.5° to 35° C.); therefore, in taking the specific gravity of *freshly-voided* urine, before cooling, its temperature should be observed, and for every 7 degrees of temperature the thermometer indicates above that upon which the urinometer is standardized 1 degree should be added to the specific gravity of the urine in addition to that indicated by the urinometer. This is important in the case of the older urinometers, many of which are standardized at 60° F. (15.6° C.), permitting, as will be seen, an error of 4 or 5 degrees with freshly-voided urine if the above correction be neglected.

Chemical Reaction.—Normal mixed urine—that is to say, the whole twenty-four hours' product—is always acid. The acidity is due to acid sodium phosphate, and not, as formerly supposed, to free acid. This sodium phosphate is derived from the basic sodium phosphate of the blood; the uric, hippuric, sulphuric, and carbonic acids of the urine take up part of the sodium, leaving an acid salt.

The degree of acidity of the urine varies at different times of the day, especially with regard to food. Soon after a meal the acidity begins to diminish, and in from three to four hours the alkaline tide usually reaches its height; occasionally, though rarely, the acidity may become so diminished at such times that the urine gives an alkaline reaction with test-paper. Freshly-voided urine may be alkaline either from fixed alkali (potassium or sodium) or from volatile alkali (ammonium). It is important to distinguish between these two conditions, as in the first case it merely reflects a condition of the blood, while in the second case it is nearly always associated with chronic inflammatory conditions of the lower urinary tract, notably the bladder. If red or violet litmus-paper turn blue in contact with urine just voided, and remain blue upon drying, the reaction is due to fixed alkali. If, on the other hand, the paper return to the original color upon drying, the reaction is due to volatile alkali (ammonium).

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[1] These instruments are furnished by Eimer & Amend, 205 and 211 Third Avenue, New York.

The urine is rendered alkaline by the administration of alkaline carbonates or the salts of vegetable acids. The urine may be rendered alkaline, usually to a less extent, by the following circumstances: Soon after a full meal; after the discharge of gastric juice in abnormal ways,—through fistula or by copious vomiting; after hot baths and free perspiration; upon a vegetable diet. With vegetarians, as with herbivorous animals, the food contains an excess of alkaline salts or vegetable acids. These acids are converted into carbonates in the blood, which, passing into the urine, cause an alkaline reaction.

The acidity of urine is increased by the ingestion of acids, saccharin, a purely meat diet, and prolonged muscular exercise. It may be developed, as already shown, by acid fermentation, and in certain pathological conditions free fatty acids may appear and render the urine sharply acid (lipaciduria).

Occasionally it happens that the urine is amphoteric,—*i.e.*, the same urine turns red litmus-paper blue and blue litmus red. This seemingly paradoxical reaction, according to Huppert, depends upon the presence of acid and neutral phosphates in variable proportions.

Quantity.—The average quantity of urine of a healthy individual who eats and drinks in moderation, and lives in a temperate atmosphere, is about 1500 cubic centimetres (50 ounces) in twenty-four hours. The relative quantity varies considerably with the time of day, most being passed in the afternoon, less in the morning, and least at night. The volume of urine for twenty-four hours varies much in conditions of health, according to certain circumstances. It is decreased by unusual activity of the skin and bowels, as well as by rest and abstaining from fluids. It is decidedly increased by imbibing large quantities of fluids, the use of diuretic drugs, to a less extent by cold, atmospheric moisture, exercise, and liberal eating.

Pathologically the urine is increased in diabetes, cirrhosis of the kidney, amyloid or waxy kidney, pure cardiac hypertrophy, pyelitis, hysteria, and convulsions. The quantity of urine is decreased in acute nephritis, cyanotic induration from cardiac defect, acute fevers, and inflammations. The urine may be more or less completely suppressed in the acute forms of nephritis, in the algid stage of cholera and yellow fever, by violent fevers and inflammations, by shock or collapse from internal injuries,—as rupture of the liver, spleen, bowels, or other viscera,—by the reflex shock or the septic congestion of catheterization (urinary fever), and by obstructive diseases of the urinary passages, notably the ureters. Finally, it is important to observe that in nephritis more or less complete suppression of the urine, often followed by uræmia and death, may result from the administration of anæsthetics such as chloroform and ether, notably the latter.

In estimating the quantity of urine it should be carefully collected for twenty-four hours, in an accurately-covered vessel, in order to exclude dust and prevent evaporation, the patient being directed to void and collect the urine previous to each movement of the bowels.

Solids.—In determining the solids of the urine observations should be made upon a sample of the mixed product of the kidneys for the whole twenty-four hours. The most accurate results are obtained by taking a given quantity of urine,—say, 20 cubic centimetres,—in a previously-weighed porcelain dish, and evaporating it over a water-bath. It should then be dried in a warm chamber for an hour or so, and then allowed to cool, when it should be weighed. This should be repeated a number of times until there is no further loss of weight from drying; then the difference in weight between the empty dish and that containing the dried solids constitutes the weight of the solids in 20 cubic centimetres of the urine. From this the solids of the whole volume of urine may be readily reckoned.

The foregoing method being somewhat tedious, and, besides, consuming too much time for practical work, approximate results may be more readily obtained by multiplying the last two figures of the specific gravity of the urine by the co-efficient of Häser, which is 2.33. This gives, approximately, the number of grammes of solids in each 1000 cubic centimetres of the urine.

Example.—If the twenty-four hours' urine be 1500 cubic centimetres, and the specific gravity be 1.020 with Häser's co-efficient, then we have as follows:—

$20 \times 2.33 = 46.60$ grammes in 1000 cubic centimetres of urine;

therefore, $\frac{46.60 \times 1500}{1000} = 69.9$ grammes of solids.

TABLE FOR ESTIMATING TOTAL SOLIDS FROM SPECIFIC GRAVITY.

SPECIFIC GRAVITY.	SOLIDS FOUND BY WEIGHING.	SOLIDS FOUND BY MULTIPLYING BY 0.233.
	Per Thousand:	Per Thousand:
1.0160	37.4	37.28
1.0260	62.0	60.58
1.0154	35.1	35.88
1.0261	60.2	60.81
1.0213	48.6	49.63
1.0230	56.4	53.59
1.0225	49.3	52.42
1.0240	54.1	55.92
1.0257	60.4	59.88
1.0275	63.9	64.07
1.0217	48.5	50.56
1.0223	52.15	51.96
1.0140	31.08	32.62
1.0236	56.64	54.98
1.0133	30.87	30.99
1.0134	31.06	31.22
1.0238	57.09	55.45
1.0250	60.47	58.25
1.0164	37.26	38.21
1.0135	33.35	31.45
1.0210	48.54	48.93
1.0137	32.55	31.92
1.0085	19.16	19.80
1.0110	24.96	25.63
	Average:	
1.0200	46.59	46.52

From these determinations it will be found that, by dividing the mean quantity of solid constituents found in 1000 grammes of urine by the last three decimals of the mean specific gravity, we obtain the quotient 0.23295, for which we may conveniently substitute the number 0.233, as Häser suggests. By multiplying with this quotient the three last decimals of the specific gravity carried out to four places of decimals, we obtain the figures in the third column of the table. The variations from the results obtained by actual weighing may be seen by a glance at the table. If, however, as is usual, the specific gravity of the urine be determined only to three decimals, the second and third figures multiplied by 2.33, as suggested by Häser, give approximately the amount of solid matters in 1000 parts of urine.

A material reduction of the solids of the urine in cases of renal disease indicates a tendency to uræmia, and therefore puts the physician on his guard against this dangerous complication. The diagnosis between diabetes insipidus and hydruria may be determined by the amount of solids in the urine. The so-called *renal inadequacy*—an unscientific term introduced by Sir Andrew Clark, which usually means unrecognized interstitial nephritis—and the *anazoturia* of Willis are both indicated by a reduction of the solids of the urine.

During the course of acute fevers and inflammations the quantity of solids in the urine furnishes very valuable information as a guide both for prognosis and treatment. The amount of tissue metamorphosis, as evidenced by the quantity of solids in the urine, is a good indication of the severity of the disease. If these changes be too active, measures are indicated for restraining them. If exudations are to be removed, a copious excretion may indicate to us that the chemico-vital changes ending in elimination are progressing sufficiently without artificial aid. Again, by insufficiency of the urinary solids defective elimination may be detected when the thermometer indicates a high ratio of tissue metamorphosis in progress, and we are thereby admonished to employ measures to re-establish elimination.

No definite deductions are to be drawn, from the quantity of solids present, as to the relative amount of any special product, especially that of urea. Since the amount of urea normally constitutes about one-half of the solids excreted by the kidneys, it has been suggested that an approximate knowledge of the amount of urea is to be gained by merely dividing the whole quantity of solids by 2. Such a rule should never be suggested as a guide in pathological conditions, because, under such circumstances, the various solids of the urine are often present in widely different *proportions*, as well as quantities. In addition to this, the special solid constituents of the urine possess widely different specific gravity,—notably that of urea from sodium chloride, which is as 2 to 3. For these reasons, even when the total solids are determined with accuracy, the amount of urea, nitrogen, or other constituent, if sought, can only be determined by special quantitative methods, which will be described in the succeeding section of this work.

Having ascertained the actual quantity of solids in the urine, in order to make deductions therefrom of any definite value in health or disease, careful regard must be had to certain conditions and features connected with each individual case before we can determine the degree in which the quantity of solids is excreted above or below the average or normal standard for such individual case. Those that chiefly influence the normal balance of excretion can be reduced to a ratio that will afford approximate results of definite and practical value. The most prominent of these conditions are: the weight of the individual, the age, the diet, and the amount of exercise taken. We may place the average weight at 66 kilogrammes (145 pounds) avoirdupois, the age being from 20 to 40, the diet that of ordinary mixed foods, and the exercise being that of the usual healthy man about ordinary labor. To the above standard the following general rules may be applied:—

1. The average excretion of solids per weight of 145 pounds being 61.14 grammes (945 grains), a proportional reduction or addition should be allowed, according to the weight of the subject examined.

2. Deduct 10 per cent. from the average solids in persons between 40 and 50 years of age, 20 per cent. if between 50 and 60, 30 per cent. if between 60 and 70, and 50 per cent. above 70.

3. *For Diet.*—In persons who have fasted for two or more

days, as in some fevers and other diseases, deduct one-third from the average solids. If the diet be spare, deduct one-eighth to one-sixth; if rather plentiful, but still below that of health, deduct one-tenth.

4. *For Exercise.*—If there be total rest, deduct one-tenth from the average solids; but if merely quietude, deduct one-twentieth.

The average standard of excretion of solids by the kidneys (61.14 grammes—945 grains—for weight of 66 kilogrammes—145 pounds avoirdupois) represents the mean of the combined observations by Becquerel, Parkes, Bocker, J. Vogel, Lehman, Gorup Besanez, Ranke, and Rummel, obtained by evaporating the urine and determining the solids by actual weighing. The rules for correction are based on the proportions laid down by Parkes.

SECTION II.

COMPOSITION OF NORMAL URINE.

ORGANIC CONSTITUENTS.

UREA—$CO(NH_2)_2$.

UREA, or carbamid, was first prepared synthetically from ammonium cyanate—$(NH_4)CNO$—by Wohler (1828). From the urine it was first prepared in an impure state by Rouelle, and subsequently by Fourcroy and Vanquelin. Urea crystallizes in colorless, quadrilateral, or six-sided, silk-like prisms with oblique ends, or, when rapidly crystallized, in delicate white needles, which melt at 120° C. (248° F.). They contain no water of crystallization, and are permanent in the air, soluble in cold water, the solution being neutral in reaction. With nitric acid urea unites to form nitrate of urea ($CON_2H_4HNO_3$), which crystallizes out in octahedral, lozenge-shaped, or hexagonal plates, which are less soluble in water than are urea crystals.

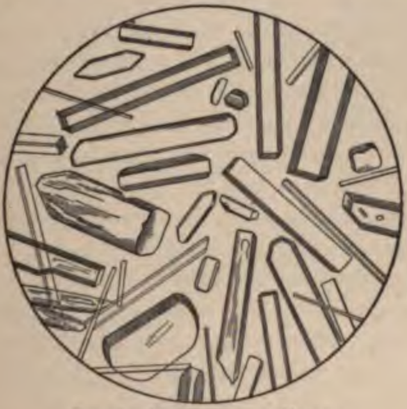

FIG. 2.—CRYSTALS OF UREA.

Urea owes its origin in the economy partly to retrograde tissue metamorphosis, including the blood, and partly to splitting up of unassimilated nitrogenous principles of the food. Thus, the greater portion of nitrogen taken into the system in the way of food is excreted by the kidneys in the form of urea. It is therefore the most bulky single constituent of the urine, ranging in quantity, according to circumstances, from 20 to 40 grammes (300 to 600 grains) in twenty-four hours in the healthy adult.

That the liver constitutes the chief seat of urea formation is now pretty generally accepted as fact. This was originally claimed to be the case by Meissner, and more recently confirmed by Brouardel, Schroeder, and Minkowski. It is not improbable, however, that the spleen and perhaps the lymphatic and secreting glands to some extent participate in the urea formation. Formerly it was erroneously supposed that urea was formed in the kidneys; but it is now known that after complete extirpation of the kidneys the formation of urea continues as before, and accumulates in the blood. Likewise, in diseases of the kidney entailing suppression of the urine, urea continues to be formed and accumulates in the organism. The evidence derived from pathology strongly points to the liver as the chief seat of urea formation. Thus, in diabetes, we know that metabolism of the hepatic cells is greatly increased, causing an abundant formation of sugar as well as urea, which pass into the blood and are excreted by the kidneys. On the other hand, in degenerative changes in the liver the urea formation is markedly diminished. Thus, in acute yellow atrophy of the liver the urea in the urine is greatly diminished—sometimes absent. The relations of degenerative changes in the liver to urea formation have recently been much elucidated by Noel Paton,[1] who points out that two functions of the liver exist—bile formation and urea formation—and, moreover, that they bear a direct relationship to each other. It has already been stated that urea owes its origin in the economy to retrograde tissue metamorphosis and nitrogenous principles of the food; in other words, the proteid constituents in the organism. Of the intermediate steps in this transformation but little is definitely known, although much has been written on this subject, most of which is conjectural. The excretion of urea reaches its maximum quantity upon an exclusive meat diet; much less is excreted upon a mixed diet, and least of all upon a strictly vegetable diet.

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[1] British Medical Journal, vol. ii, 1886, p. 207.

Variations in the quantity of urea excreted, in a measure, constitute an expression of the changes in nitrogenous tissue metabolism, and as such possess definite clinical value. Thus, in acute fevers and inflammations, until the crisis of the disease is reached there is greatly increased elimination of urea. On the other hand, in chronic diseases (cachexias), when tissue metamorphosis is retarded through malnutrition, the excretion of urea is diminished. Similar results follow in diseases involving the integrity of the liver,—the elaborating source of urea. In Bright's disease urea excretion is diminished in consequence of impairment of the structure of the kidneys. Preceding, usually for some time and during uræmic attacks, the excretion of urea is markedly diminished, forming a valuable indication of the approach of this dangerous complication. Mental and muscular activity hasten urea excretion by accelerating tissue waste; and hence urea excretion is more active during waking than during sleeping hours. The variations in the amount of exercise, the quantity and quality of food taken, atmospheric vicissitudes, the degree of activity of the other excretory organs, etc., render the relative and absolute amount of urea excreted almost as variable as the amount of water. If the mode of life be very regular and equable, the amount remains pretty uniform; but great care is necessary to maintain all the physiological conditions even. Under the latter circumstances the mean amount of urea excreted in twenty-four hours, by healthy adult males between the ages of 20 and 40 years, is 33.18 grammes (512.4 grains). Close calculations give the average excretion of urea as .015 to .035 gramme per hour for each kilogramme of body-weight. The absolute quantity of urea excreted by women is below the average of men. The same is true with children; but, on the other hand, the relative quantity excreted by children is much higher than by either men or women.

Urea may be separated from the urine as follows: First evaporate, then add strong, pure nitric acid in excess, keeping the mixture cool during acidulation. Pour off the excess of fluid from the crystals of urea nitrate formed; strain through muslin and press between heavy filter-paper. Add to the dry product barium carbonate in excess, and add sufficient alcohol to form a pasty consistence. Dry on a water-bath, and extract with alcohol; filter; evaporate the filtrate on a water-bath, and set aside to crystallize. The result is nearly pure urea, plus the coloring matters of the urine. The simplest method of decolorizing the product is to filter through animal charcoal, and afterward purify by recrystallization.

Detection.—1. A very simple method of detecting urea is to place a drop or two of the suspected fluid upon a glass slide, and after adding a drop of nitric acid gently warm over a spirit-lamp. If urea be present, upon evaporation the microscope will show the characteristic crystals of nitrate of urea, of rhombic or hexagonal forms, singly or in masses, their acute angles being eighty-two degrees.

2. Add to the suspected fluid three parts of an aqueous solution of furfur aldehyde, and subsequently a few drops of strong hydrochloric acid, and warm. A series of colors—yellow, green, violet, purple, and red—is produced, settling at length into a brown, sticky mass if urea be present.

3. To a few drops of the suspected fluid in a test-tube add an equal quantity of solution of hypobromite of sodium, and a rapid evolution of bubbles takes place if urea be present.

4. Warm a few crystals of urea in a test-tube; add a trace of caustic sodium or potassium and a drop of a dilute solution of cupric sulphate. A violet or rose-red color is produced,—the biuret reaction.

Determination of Urea.—The methods devised for the purpose of determining the quantity of urea in the urine are very numerous; most of which, however, are founded upon one of three principles: 1. The mercuric nitrate, or Liebig's method. 2. The hypobromite, or Knop-Hufner method. 3. The differential density method, obtained by measuring the amount of urea by the specific gravity of the urine lost through decomposition of the contained urea.

Liebig's Method.—The combination between urea and mercuric oxide—$(CON_2H_4)_2 Hg (NO_3)_2 + 3 HgO$—forms a white precipitate, insoluble in water and weak alkaline solutions. It is, therefore, necessary to prepare a standard solution of mercury, and to have an indicator by which to detect the point when all the urea has entered into combination with the mercury, the latter slightly predominating. This indicator is sodium carbonate, which gives a yellow color with the excess of mercury, in consequence of the formation of hydrated mercuric oxide.

Theoretically, 100 parts of urea should require 720 parts of mercuric oxide; but practically 772 parts of the latter are necessary to remove all the urea, and at the same time to show the yellow color with alkali; therefore, the solution of mercuric nitrate must be of empirical strength in order to give accurate results. The following solutions are required for testing:—

1. Standard mercuric nitrate solution. Dissolve 77.2 grammes (1158 grains) of red oxide of mercury (weighed after drying over a water-bath), or 71.5 grammes (1072 grains) of the metal itself in dilute nitric acid. Expel the excess of acid by evaporation to a syrupy consistence. Make up to 1000 cubic centimetres with distilled water, adding the water gradually. This solution is of such strength that 19 cubic centimetres will precipitate 10 cubic centimetres of a 2-per-cent. urea solution. Add 52.6 cubic centimetres of water to the litre of the mercuric nitrate solution, and shake well; then 20 cubic centimetres (instead of 19) equal 10 cubic centimetres 2-per-cent. urea solution,—*i.e.*, 1 cubic centimetre equals 0.01 urea.

2. Baryta mixture. Prepare by mixing two volumes of solution of barium hydrate with one volume of solution of barium nitrate, both saturated in the cold.

Analysis.—Take 40 cubic centimetres of urine, add to this 20 cubic centimetres baryta mixture and filter off the precipitate of baryta salts (phosphates and sulphates). Take 15 cubic centimetres of the filtrate (corresponding to 10 cubic centimetres of urine) in a beaker. Discharge into it the mercuric nitrate solution from a burette, until, on mixing a drop of the mixture with a drop of saturated solution of sodium carbonate on a white tile, a pale-lemon color appears. Then read the amount used from the burette, and calculate thence the percentage of urea.

Corrections.—This method only approaches accuracy when the quantity of urea present is about 2 per cent.,—the normal percentage of urea in the urine. The chlorine in the urine must be estimated, and the quantity of urea indicated reduced by subtraction of 1 gramme (15 grains) of urea for every 1.3 grammes (19 grains) of sodium chloride found. If the urine contain less than 2 per cent. of urea, 0.1 cubic centimetre of mercuric nitrate solution must be deducted for every 4 cubic centimetres used; if more than 2 per cent. of urea, a second titration must be performed, with the urine diluted with half as much water as has been needed of the mercurial solution above 20 cubic centimetres. Suppose, then, 28 cubic centimetres have been used in the first titration, the excess is 8 cubic centimetres; therefore, 4 cubic centimetres of water must be added to the urine before the second titration is made. When ammonium carbonate is present, first estimate the urea in one portion of urine, and the ammonium by titration with normal sulphuric acid in another; 0.017 gramme of ammonium equals 0.030 gramme of urea. The equivalent of ammonium in terms of urea must be added to the urea found in the first portion of the urine.

Modifications.—Rautenberg[1] and Pflüger[2] have devised the following modifications of Liebig's original method, just described:—

Rautenberg's method consists in maintaining the urea solution neutral throughout by successive additions of calcium carbonate.

Pflüger's modification is the one most generally employed, which is as follows: A 2-per-cent. solution of urea is prepared; 10 cubic centimetres of this are placed in a beaker, and 20 cubic centimetres of the mercuric nitrate solution are run into it in a continuous stream; the mixture is then placed under a burette containing normal sodium carbonate, and this is added, with constant agitation, until a permanent yellow color appears. The volume so used is noted as that necessary to neutralize the acidity produced by 20 cubic centimetres of the mercurial solution in the presence of urea. A plate of glass is then laid on black cloth, and some drops of a thick mixture of sodium bicarbonate

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[1] Ann. Chem. Pharm., vol. cxxxiii, p. 55.

[2] Zeit. anal. Chem., vol. xix, p. 375. Pfeiffer (Zeit. Biol., vol. xx, p. 540) has carefully compared the different methods.

(free from carbonate) and water placed upon it at convenient distances. The mercurial solution is added to the urine in such volume as is judged appropriate, and from time to time a drop of the white mixture is placed beside the bicarbonate, so as to touch but not mix completely. A point is at last reached when the white gives place to yellow; both drops are then rubbed quickly together with a glass rod, and the color disappears; further addition of the mercury is then made to the urine till a drop rubbed with the bicarbonate remains permanently yellow. Now neutralize by the addition of the normal sodium carbonate to near the volume found necessary in the preliminary experiment. If this be quickly done, a few tenths of a cubic centimetre of mercuric nitrate will be found sufficient to complete the reaction. If much time has been lost, however, it may occur that, notwithstanding the mixture is distinctly acid, it gives, even after the addition of sodium carbonate, a permanent yellow, although no more mercuric nitrate be added. The analysis, under such circumstances, must be repeated, taking the first titration as a guide to the quantities which are necessary. Pflüger's correction for concentration of urea is different from Liebig's, and is as follows:—

$V^1 =$ volume of urea solution + volume of sodium-carbonate solution + volume of any other fluid free from urea which may be added.

$V^2 =$ volume of mercuric nitrate solution used.

$C =$ correction $= -(V^1 - V^2) \times 0.08$.

This formula holds good for cases in which the total mixture is less than three times the volume of mercuric nitrate solution used; with more concentrated solutions the formula gives results too high.

Hypobromite Method.—This is a far more simple and ready method to manipulate. The principle of the method introduced by Knop depends upon the fact that, when urea in solution comes in contact with sodium-hypobromite solution, nitrogen is set free as a result of the total decomposition of the urea. Thus:—

$$CH_4ON_2 + 3NaBrO = CO_2 + 2H_2O + 3NaBr + 2N.$$

The CO_2 is absorbed by the sodium-hydroxid solution. One gramme of urea furnishes 370 cubic centimetres of nitrogen at 0° C and under 760 millimetres pressure. Knop's hypobromite-of-sodium fluid is made as follows: In 250 cubic centimetres of distilled water 100 grammes of caustic sodium are dissolved, and after cooling 25 cubic centimetres of bromine are added.

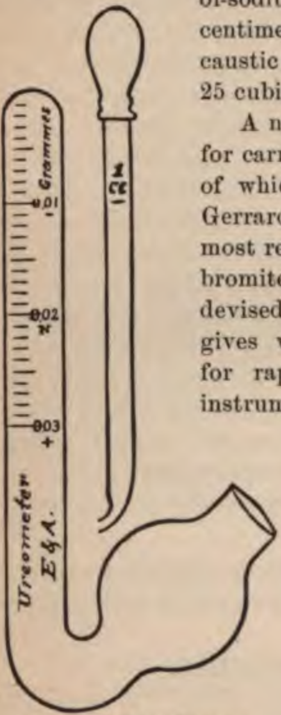

FIG. 3.—DR. DOREMUS'S UREOMETER.

A number of apparatuses have been devised for carrying out this method, the best known of which are those of Hufner, Dupré, and Gerrard. But altogether the simplest and most ready method of carrying out the hypobromite test is by means of the instrument devised by Doremus, of New York, which gives very satisfactory approximate results for rapid clinical work.[1] The bulb of the instrument is filled with the alkaline hypobromite solution, and by inclining the tube the long arm is filled to the bend at the bulb.[2] By means of the nipple-pipette, 1 cubic centimetre of the urine to be tested is slowly discharged up the long arm into the hypobromite solution. A rapid decomposition of urea takes place; the bubbles of nitrogen rise in the long arm of the instrument, while the displaced liquid flows into the bulb, which serves as a reservoir for the overflow. In fifteen minutes the decomposition of urea is complete, and the graduation on the long arm will indicate the quantity of urea in the volume of urine tested. Two forms of the instrument are furnished,—one graduated to read fractions of a gramme to the cubic centimetre of urine, and the range is from 0.01 to 0.03 gramme. If it be desired to read the percentage of urea instead of the grammes per cubic centimetre, simply remove the decimal-point two figures to the right,—thus, 0.02 gramme to the cubic centimetre is 2.0 per cent. of urea. The other form of the instrument is similar, save that it is graduated to show the number of grains of urea per fluidounce of urine.

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[1] Messrs. Eimer & Amend, 205 and 211 Third Avenue, New York, supply these instruments at very moderate cost.

[2] As the hypobromite solution does not keep well, it is best to keep the bromine and the caustic-sodium solution separate, as follows: Have on hand a solution of sodium hydroxid, 100 grammes to 250 cubic centimetres of water (6 ounces to the pint). In another bottle should be kept the bromine. To prepare the solution freshly for use, take 10 cubic centimetres of the sodium-hydroxid solution, and add thereto 1 cubic centimetre of bromine (1 to 10). After the bromine has been thoroughly mixed with the alkali, dilute with an equal volume of water, and the solution is ready for testing.

The normal quantity of urea in the urine is about 2 per cent., or 0.02 gramme per cubic centimetre, or 10 grains per ounce.

The *differential density method*, as devised by Dr. George B. Fowler, of New York, is very simple in application. This method is based upon the fact that there is a difference in the specific gravity of urine before and after the decomposition of its urea by the hypochlorites. Every degree of density lost corresponds to 0.77 per cent., or about 3½ grains per ounce. The hypochlorite solution employed is Squibb's solution of chlorinated sodium (Labarraque's solution), of which seven parts will destroy the urea in one part of urine, unless the amount is very large, in which case the urine should be diluted with an equal bulk of water and the result multiplied by 2. The process consists in adding to one volume of urine—say, one ounce in a large hydrometer jar—seven volumes of Labarraque's solution. Decomposition immediately ensues, and at the expiration of a few hours all the nitrogen of the contained urea has escaped. The specific gravity of the quiescent mixture is now noted, and also that of the pure urine. We now have the specific gravity of the mixture of the urine and Labarraque's solution after decomposition. In order to ascertain what it was before decomposition, we resort to the law of proportions. Multiply, therefore, the specific gravity of the Labarraque solution by 7, add the specific gravity of the urine, and divide the sum by 8. Now, from this—the specific gravity of the mixture before decomposition—subtract that obtained after decomposition. Multiply the difference in degrees by $3\frac{1}{2}$, and the result will be the number of grains of urea per ounce of urine; or, better, by 0.77, which gives the percentage of urea. The presence of sugar or albumin in the urine does not interfere with this test.

URIC ACID ($C_5H_4N_4O_3$).

Uric acid, like urea, is a nitrogenous product, although it exists in the urine in comparatively small amount,—about 0.4 to 0.8 gramme being excreted by the kidneys in the healthy man in twenty-four hours. Upon decomposition uric acid yields about 33.3 per cent. of its weight in nitrogen. It is feebly soluble, requiring 15,000 parts of cold or 1900 parts of boiling water to dissolve it. It is, for the above reason, rarely found in the urine in the free state; more often in the form of crystalline deposit,—reddish sand; most often, however, it exists in combination as urates.

Uric acid is dibasic; that is to say, it contains two atoms of H which may be substituted by two atoms of a monad metal. Urates containing but one atom of potassium, sodium, or ammonium are acid urates; those containing two atoms are neutral salts. The neutral salts of uric acid are readily soluble in water, while the acid salts are but feebly so. The above fact explains the reason why nearly all urate deposits consist of acid urate salts; their feeble solubility permits them to fall out of solution as the urine cools. If the urine remain clear for some time after cooling, we may infer that the contained urates are in the soluble form of neutral urate, the alkaline base predominating. When a strong acid is added to such a urine,—especially if the urates be present in excess,—the acid unites with the excessive base and forms an acid urate, which, on account of its relatively feeble solubility, is at once precipitated in finely-granular form, producing a whitish opacity. This explains the occasional action of the nitric-acid test for albumin when the urine is highly charged with neutral urates.

Uric acid crystallizes in the urine in rhombic, rectangular prisms, wedge- and whetstone- shape, of yellowish-red color, constituting, with its salts, the only sediments of the urine thus colored.

Uric acid corresponds with urea in its protein origin in the organism, but the seat of its formation has given rise to much discussion. Two different views are held upon this subject: 1. That, like urea, it is formed in the tissues, notably in the spleen and liver, and merely excreted by the kidneys. This view is supported by the following facts: (*a*) In the normal condition but a small amount of uric acid is found in the blood. (*b*) In gout, where excretion of the uric acid is diminished, it accumulates in the blood and tissues. (*c*) After extirpation of the kidneys it continues to be formed. (*d*) The secretion of uric acid is most abundant at the period of digestion, when the liver and spleen are the most active. 2. This view supposes that the kidneys not only constitute the seat of excretion, but also that of formation of uric acid. Garrod has ably supported this view,[1] basing his conclusions, first, on the fact of the small amount of uric acid in the blood of birds and reptiles, and also that he was unable to find more uric acid in the liver and spleen of birds than in those organs in mammals. But Schroeder has recently shown (1) that the liver of birds contains a high percentage of uric acid; (2) that after removal of the kidneys uric acid continues to be formed, and accumulates in the blood and liver; (3) that by passing blood through the liver, immediately after removal of that organ from the body, it is found that the uric acid is much increased; and (4) he regards ammonia as the most important precursor of uric acid, just as in mammals it is the most important precursor of urea.[2] In addition to this, the experiments of Minkowski are still more conclusive. He succeeded in keeping geese alive for from six to twenty hours after extirpation

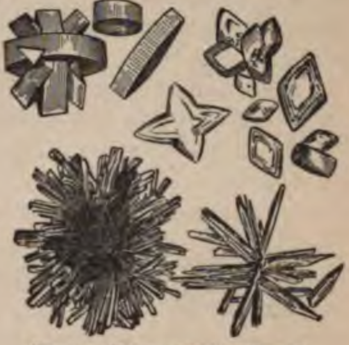
FIG. 4.—URIC-ACID CRYSTALS. (After Kuhn.)

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[1] Lumleian Lectures, Lancet, vol. i, 1883.

[2] Ludwig's Festschrift, 1887, p. 89.

of the liver; after the operation their urine contained but 2 or 3 per cent. of uric acid, instead of the normal 60 or 70 per cent.; the ammonium was correspondingly increased to 50 or 60 per cent., instead of the normal 9 to 18 per cent.

All the facts at present available render the following conclusions probable: 1. That uric acid is formed chiefly in the liver. 2. It is formed by the synthesis of ammonium and lactic acid, which, after the removal of the liver, appear in the urine in equivalent quantities. 3. That the remnant of uric acid in the urine after extirpation of the liver originates from xanthin and similar products.

The quantity of uric acid in the urine should never be presumed to be excessive from the mere fact of deposit of uric-acid crystals in the urine upon cooling, as in fact such may, and very often does, occur when the uric acid is both relatively and absolutely deficient. The conditions of the urine which tend to precipitation of uric acid are as follow: 1. High grade of acidity of the urine. 2. Poverty in mineral salts. 3. Low percentage of pigmentation. 4. High percentage of uric acid. 5. Long standing. Any urine upon standing sufficiently long will deposit uric-acid crystals in consequence of the changes culminating in ammoniacal decomposition.

As already stated, the quantity of uric acid excreted in twenty-four hours by the average healthy man ranges from 0.4 to 0.8 gramme (7 to 10 grains). The proportion of urea to uric acid is stated by Parkes to be about 45 to 1.

Uric-acid excretion is increased by a rich animal diet, especially if combined with limited exercise in the open air; by acute febrile conditions; by lung and heart diseases, attended by dyspnœa; by diseases which impede respiration, as large abdominal tumors, ascites, etc.; by leukæmia; and by the so-called uric-acid cachexy. Uric acid, on the other hand, is diminished in advanced Bright's disease, urina spastica, hydruria, arthritis (especially the gouty form), gout, and, in general, wherever urea is diminished in quantity uric acid is usually also diminished.

Detection of Uric Acid.—1. Uric acid, as such, is easily recognized by the microscope, owing to the characteristic rhombic, yellowish-red crystals. The microscope also most readily distinguishes uric acid from its compounds.

2. The presence of both uric acid and its compounds may be readily detected by means of the *murexide test.* The sediment, or residue, after evaporation, is first treated with a few drops of nitric acid in a porcelain capsule, and, after warming over a spirit-lamp until evaporated almost to dryness, a drop or two of ammonium is added, and, if present, a beautiful purple-red color immediately appears, gradually diffusing over the bottom of the capsule.

The murexide test depends upon the facts that, by the addition of nitric acid and heat to uric acid or urates, first alloxan and subsequently alloxantin are formed, which, on the addition of ammonium, form murexide,—acid purpurate of ammonium.

3. If one or two drops of nitrate-of-silver solution be dropped upon white filter-paper, and then touched with an alkaline solution of uric acid (sol. with sodium carbonate), a black color appears if 0.001 per cent. of uric acid be present; even 0.0005 per cent. of uric acid, if present, will cause a brownish-yellow or grayish stain.

4. A solution of uric acid or urate, warmed with copper sulphate and caustic potassium, produces a reddish precipitate of cupric oxide.

Determination of Uric Acid.—An approximate and sufficiently accurate process for most clinical purposes is Heintz's method, which is also very simple: Take 200 cubic centimetres of urine, and add to it 10 cubic centimetres of hydrochloric acid. Let stand for twenty-four hours in a cool room. Collect the precipitated uric-acid crystals on a previously-weighed filter, and wash with cold distilled water. Dry the filter and uric-acid crystals in a desiccator, and weigh. By subtracting the weight of the filter, the result will be the weight of the uric acid in 200 cubic centimetres of urine. If albumin be present, it should first be coagulated by a few drops of acetic acid and heat, and then filtered off.

Occasionally it happens that urine containing uric acid gives no precipitate as above, and a number of other methods have been suggested, but as yet we lack a thoroughly trustworthy and ready method for clinical work. Haycraft's method has heretofore been most employed. This is based upon the fact that uric acid combines with silver as silver urate; the silver urate is collected, dissolved in nitric acid, and the silver is estimated volumetrically by Vollard's method. From the amount of silver found the amount of uric acid is calculated. Czapek found a large error in this method, and Salkowski also regards the process as misleading, because the composition of the silver urate is not uniform, and Gossage confirms this statement. The methods of Fokker-Salkowski and Camerer have been strongly recommended, of late. The following method of Hopkins, which is a modification of Fokker's method, has recently been recommended as the best to date[1]:—

Hopkins's Method.—In this process the uric acid and all the urates are precipitated by saturation with ammonium chloride, which converts them all into urates of ammonium. They are then filtered out and the uric acid separated by the action of hydrochloric acid. The final estimation is then made by titration with a standard solution of potassium permanganate, which is found more accurate than weighing.

The process, as applied to all urines, normal and pathological, is as follows:—

1. *In Normal Urine without Deposit.*—(*a*) To 100 cubic centimetres of the urine ammonium chloride is added until practically saturated; about 50 grammes are necessary. When a small quantity of the chloride remains undissolved, even after brisk stirring at intervals of a few minutes, saturation is sufficient. As the temperature of the urine again rises, from the depression due to the process of solution, any residual crystals will, for the most part, dissolve; but there is no necessity for adding more.

(*b*) After having stood for two hours,—better with occasional agitation, to promote subsidence,—the precipitate produced is filtered through a thin filter-paper and washed three or four times with saturated solution of ammonium chloride. The filtrate should remain perfectly clear and bright.

(*c*) With a jet of hot distilled water the urate, which will be somewhat pigmented, is now washed off the filter into a small beaker, and heated just to boiling with an excess of hydrochloric acid. It is then allowed to stand for the uric acid to separate out completely. Two hours is sufficient, if the liquid be cooled. The acid is then filtered off and washed with cold distilled water. The filtrate should be measured *before* the washing has begun, and 1 milligramme added to the final result for each 15 cubic centimetres of liquid present. This need never be more than from 20 to 30 cubic centimetres.

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[1] Jour. Pathology and Bacteriology, 1893, vol. i, No. 4, p. 450.

The acid is now again washed off the filter with hot water, warmed, with the addition of sodium carbonate, till dissolved, and the solution then made up to 100 cubic centimetres. Being transferred to a flask of sufficient capacity, it is mixed with 20 cubic centimetres of strong, pure sulphuric acid, and immediately titrated with one-twentieth normal potassium-permanganate solution. The latter should be added slowly toward the end of the reaction, the close of which is marked by the first approach of pink color, which is permanent for an appreciable interval. Previously, the disappearance of the color will have been instantaneous. The flask should be agitated throughout the operation.

The standard solution is made by dissolving 1.578 grammes of pure potassium permanganate in 1 litre of distilled water. Of this, 1 cubic centimetre is equal to 0.00375 gramme of uric acid. The addition of 20 per cent. of sulphuric acid to the solution produces a temperature suitable to the reaction, and no thermometer need be used.

2. *In acid urine containing cystin* the author recommends the addition of a few drops of free ammonium, which will obviate all difficulty.

3. *In alkaline urine with abundance of phosphates*, they should be filtered off after complete precipitation by heat. The ammoniacal urate comes down more rapidly in alkaline than acid urine. The only objection to adding ammonium in all cases is its tendency to precipitate the phosphates.

4. *Albuminous urine* does not interfere with accurate determination of uric acid by this method, but requires a little longer digestion with hydrochloric acid.

5. *With highly-pigmented urine* the original urate precipitate

is thoroughly digested with alcohol, and after acidification the filtrate is gradually heated to boiling, and then digested for some time on a water-bath. The separated crystals are then thoroughly washed.

In all cases exceedingly accurate results are claimed, and the process can be carried out with ease and comparative rapidity.

XANTHIN ($C_5H_4N_4O_2$).

This substance contains one atom of oxygen less than uric acid, hence its close alliance chemically with the latter. Xanthin is present in normal urine, although in very small quantity. Neubauer found only 1 gramme in 300 litres of normal human urine. When deposited in the urine spontaneously, it forms brittle scales of yellowish-white color and of somewhat waxy consistence. It is insoluble in alcohol and ether, feebly soluble in water, and readily soluble in alkalies, as well as in dilute nitric and hydrochloric acids. Xanthin is a constituent of a very rare form of calculus, having thus been met with not to exceed half a dozen recorded times, and these always in cases of youth. As a urinary sediment it has been encountered more frequently.

Although xanthin is widely distributed throughout the economy, having been found in most of the viscera as well as in the blood, the conditions which give rise to its increased and decreased excretion by the kidneys, as well as its occurrence as a urinary sediment, are as yet but little known. Durr and Strohmyer state that its amount in the urine is increased by sulphur-baths.

Detection.—When dissolved in dilute hydrochloric acid, upon evaporation xanthin separates into hexagonal crystals. When evaporated to dryness with nitric acid, a yellow residue remains, which turns red with caustic potassium and reddish violet on being heated.

ALLANTOIN ($C_4H_6N_4O_3$).

This substance is obtainable from uric acid by oxidation with potassium permanganate (care being taken that the temperature does not rise), the potassium permanganate taking up water and oxygen, forming allantoin and carbonic acid:—

$$\underset{\text{Uric acid.}}{2C_3H_4N_4O_2} + 2H_2O + O_2 = \underset{\text{Allantoin.}}{2C_4H_6N_4O_3} + 2CO_2.$$

Allantoin crystallizes in colorless prisms, which are soluble in hot water, but slightly soluble in cold water, and insoluble in alcohol and ether. It is precipitated from its solutions by mercuric salts. Allantoin occurs in mere traces in normal human urine, except directly after birth, but it is increased by a meat diet, and by administration of tannic acid. It was found by Wohler in the urine of newborn calves, and since then by numerous observers in the urine of newborn infants. Its close chemical alliance with uric acid is shown by the fact that Salkowski found allantoin with urea and oxalic acid much increased in the urine of animals (dogs) by the administration of uric acid.

Detection and Determination.—Allantoin may be separated from the urine by precipitation with lead acetate, filtering, passing sulphuretted hydrogen through the filtrate, filtering again, evaporating the final filtrate to a syrupy consistence, and letting it stand for several days. Allantoin then crystallizes out.

CREATININ ($C_4H_7N_3O$).

Creatinin and creatin are both constituents of normal urine, and are subject to interchange one into the other, according to certain conditions. In alkaline urine creatin appears in greater quantity, while the reverse is the case with strongly acid urine. Physiologically they may be considered as one body, although chemically they differ in the fact that creatin contains H_2O more than creatinin, as may be seen by their formulæ,—creatinin, $C_4H_7N_3O$; creatin, $C_4H_9N_3O_2$. Since the urine is usually acid, creatinin is generally considered the normal constituent.

Creatinin is a decided base—probably the strongest in the economy—giving a distinctly alkaline reaction with test paper. It crystallizes in large colorless prisms, soluble in water and alcohol, but almost insoluble in ether.

Creatinin is a constant constituent of normal human urine, being excreted in nearly the same amount as uric acid,—0.05 to

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0.09 gramme in twenty-four hours (7 to 10 grains). It has been generally considered that creatinin of the urine arises from the creatin of the muscles, because when animals are fed on creatin the creatinin of the urine is increased. But Meissner has shown that when creatin is injected into the blood it appears in the urine as such unchanged; and it would therefore appear that the kidneys have not the power of converting creatin into creatinin; the change probably takes place normally in muscles, the creatinin entering the blood and being excreted by the kidneys. Bunge, however, points out the fact that the relatively small excretion of creatinin cannot account for the large amount of creatin of the muscles,—90 grammes. He therefore considers it more probable that creatinin is ultimately converted into urea, the creatinin of the urine—or creatin, if the urine be alkaline—being derived from the food.

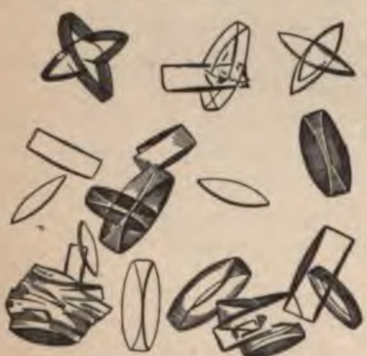
FIG. 5.—CREATININ CRYSTALS. (After Kuhn.)

Creatinin is excreted in increased amount upon a meat diet, and in diminished quantity by fasting. Clinically it is excreted in increased quantity in acute diseases,—as pneumonia, the efflorescent stages of typhoid and intermittent fever, and in some cases of diabetes, though not in all. It is diminished in convalescence from acute diseases, in advanced degeneration of the kidneys, and tetanus. In diseases characterized by muscular wasting in general, creatinin is usually diminished.

Detection and Determination.—1. When a solution of sodium nitro-prussiate is added to a dilute solution of creatinin, and subsequently sodium hydroxid is added, a red color appears, which changes to yellow upon standing (Weyl's test). 2. A solution of creatinin, as in the urine, acidulated with nitric acid, gives, with phospho-molybdic acid, a yellow crystalline precipitate, soluble in hot nitric acid. 3. With zinc chloride it gives a characteristic crystalline precipitate (groups of fine needles) consisting of a combination of zinc chloride with creatinin. This test is used for quantitative estimation of creatinin.

The five bodies just considered in detail—viz., urea, uric acid, xanthin, allantoin, and creatinin—constitute the chief constituents of normal urine of the nitrogenous type, or protein derivation. In addition to these, however, thio- (sulpho-) cyanic acid is found in the urine, in very minute quantities, in the form of thiocyanites.

AROMATIC SUBSTANCES OF THE URINE.

These comprise four classes: (*a*) Hippuric acid and similar aromatic compounds of glycocin. (*b*) Combinations of glycuronic acid with aromatic substances. (*c*) Aromatic oxy-acids. (*d*) Ethereal sulphates.

HIPPURIC ACID ($C_9H_9NO_3$).

Hippuric acid is monobasic and crystallizes either in the form of fine needles or four-sided prisms and pillars terminated by two- or four- sided beveled surfaces. The typical form is that of a vertical rhomboid prism. It is colorless, odorless, and of slightly bitter taste. It requires 600 parts of cold water to dissolve it, but it is much more soluble in hot water and readily so in hot alcohol and ether. It is soluble in ammonium and alcohol, but insoluble in hydrochloric acid. Hippuric acid is a constant element of normal urine, although present in small amount,—0.5 to 1 gramme being excreted by the kidneys in twenty-four hours.

Hippuric acid is an interesting product in a comparative physiological sense, since it forms a connecting link between the urine of herbivora, omnivora, and the carnivora; being present in comparatively large amount in the former, much less in the second, and absent in the last-named order. It is also interesting in itself, as forming one of the best illustrations of synthesis occurring in the organism.

In man the hippuric acid excreted by the kidneys depends chiefly upon the character and quantity of food eaten, being increased by a vegetable diet,—especially by certain fruits, as cranberries, prunes, green gages, etc. The administration of benzoic acid, oil of bitter almonds, toluol, cinnamic acid, benzylamin, phenylpropionic and kinic acids also cause an increased excretion of hippuric acid. On the other hand, an animal diet greatly decreases its excretion, although it does not disappear from the urine upon an exclusive meat diet. Clinically we find an increased excretion of hippuric acid in diabetes and chorea, as well as in acute febrile processes. Numerous observations go to show that hippuric acid is formed in the kidneys; synthesis, as a rule, failed after removal of these organs.

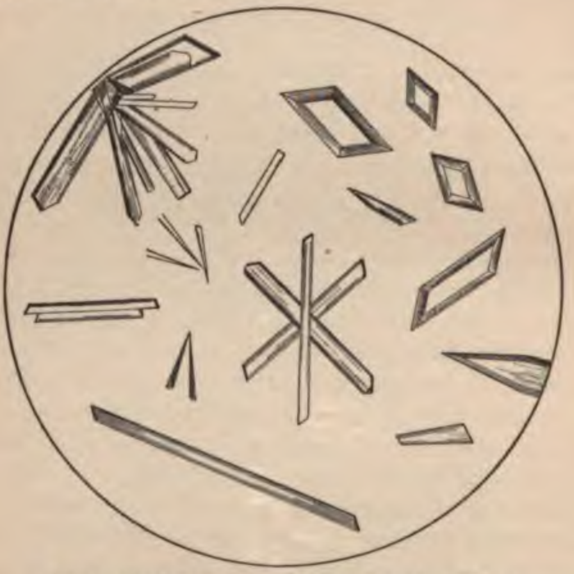

FIG. 6.—HIPPURIC-ACID CRYSTALS. (After Peyer.)

Detection and Determination.—1. Evaporate the urine with nitric acid, and heat the residue in a dry test-tube. If hippuric acid be present an odor like that of oil of bitter almonds is plainly observable, due to the formation of nitrobenzol. 2. If the urine contain an excess of hippuric acid, it may be determined by slightly evaporating and feebly acidulating with hydrochloric acid. Upon standing for a few hours the hippuric acid crystallizes out and may be recognized by the microscope. The hippuric-acid crystals may be readily separated from uric-acid crystals by hot water, if the uric acid be present in sufficient quantity to interfere with the test. 3. Meissner's method consists in precipitating carefully 1000 to 1200 cubic centimetres of urine with strong baryta-water; the excess of the latter is removed by a few drops of sulphuric acid (of which an excess is to be avoided) and then filtered. The filtrate, accurately neutralized with hydrochloric acid, is then evaporated on a water-bath to the consistency of a thick syrup, and the neutral residue, while still hot, is added to 150 or 200 cubic centimetres of absolute alcohol in a closed glass vessel. Any succinic-acid salts are precipitated together with the chloride of sodium, etc., while the hippuric-acid salts remain in solution. After repeated agitation, as soon as the precipitate has settled well the alcoholic solution is decanted and the alcohol completely driven off on the water-bath, the syrupy residue, which on cooling solidifies to a crystalline mass, is put in a closed vessel while it is still hot, acidulated with hydrochloric acid, and the hippuric acid extracted by shaking with not too small amounts of ether (100 or 150 cubic centimetres). After the ether is distilled off, the residue is diluted with water, and heated to boiling with a little milk of lime. The hippuric acid separates from the concentrated filtrate, after the addition of hydrochloric acid, in beautiful crystalline rosettes; they can be obtained entirely free from color by treating with pure animal charcoal.

Combinations of Glycuronic Acid.—This body is closely allied to the carbohydrates, and is apt to be mistaken for sugar in the urine. Normally it occurs in mere traces in urine. It occurs partly in combination with aromatic substances.

Aromatic Oxy-acids.—Of these hydroparacumaric acid or oxyphenylpropionic acid and oxyphenylacetic acid are found in minute quantities in the urine, in combination with potassium.

ETHEREAL SULPHATES.

In 1851 Stadeler discovered, on distilling the urine with dilute sulphuric acid, small quantities of phenol or carbolic acid in the distillate. Hoppe-Seyler showed that phenol is not present in the urine in a free state, but as a compound, from which it is liberated by sulphuric acid in distillation. In 1876 Baumann discovered that this compound consists of an ethereal compound of phenol and sulphuric acid. Baumann also discovered the presence of other like ethereal sulphates in the urine, consisting of compounds of the radicle HSO_3, sometimes incorrectly termed sulphonates. The most important of this series are the ethereal potassium sulphates of phenol, creosol, catechol or pyrocatechin, indole, and skatole. These compounds are present in the urine of herbivora more abundantly than in carnivora or omnivora; but they are present in the urine of all animals in smaller or larger quantities. They originate in two ways: (*a*) from aromatic substances in food, and (*b*) in the intestine as the result of putrefactive changes. In man, whose food contains but little aromatics, the origin of these ethereal sulphates is probably chiefly, if not entirely, in the intestines, as above indicated; since, if putrefaction in the intestines be arrested, these substances disappear from the urine. The proportion of the ethereal sulphates to the total sulphates of the urine is about 1 to 10.

Hoppe-Seyler found the ethereal sulphates in the urine in excess under the following circumstances: 1. In deficient absorption of the normal products of digestion, such as occurs in peritonitis and tuberculosis of the intestine, because the products of digestion undergo putrefactive changes, and the putrefactive products are absorbed. 2. Diseases of the stomach, in which the food long remains in the stomach and undergoes fermentative changes, always result in excess of ethereal sulphates in the urine. 3. Putrefactive processes outside the alimentary canal, putrid cystitis, putrid abscesses, putrid peritonitis, etc., have the same effect. The amount of ethereal sulphates is, moreover, in all cases proportional to the severity of the putrefaction, and is increased by the retention and diminished by the discharge of putrid matter; as, for instance, in opening an abscess. By these and other observations it has been conclusively established that the best guide to the occurrence and amount of putrefaction in progress in the economy is the relation of the ethereal sulphates to the total sulphates.

PHENOL-POTASSIUM SULPHATE ($C_6H_5OSO_3K$).

The above is the form in which phenol or carbolic acid exists in the urine. Phenol (C_6H_6O) was found to be one of the intestinal products of putrefaction by Baumann, as already stated.

This is absorbed and excreted in the above form; some of the sulphate comes from tyrosine, which passes through the stages of paracreosol and paraoxybenzoic acid before conversion into the phenol salt (Baumann).

After the use of carbolic acid, externally or internally, the amount of phenol sulphate in the urine is increased; two substances are formed by splitting up of carbolic acid, called pyrocatechin and hydroquinon. These become, in alkaline urine, dark brown upon exposure to the atmosphere; producing the well-known color of the urine in "carboluria."

Detection.—1. Distil the urine acidulated with sulphuric acid. Phenol appears in the distillate; add bromine-water, a precipitate of tribromophenol appears,—deep yellow. 2. Warm the distillate with Millon's reagent and a cherry-red color results. 3. Add ferric chloride to the distillate and a deep-violet color results.

Determination.—Approximate results may be obtained as follows: 100 cubic centimetres of urine are concentrated over a water-bath to 20 cubic centimetres volume. Sulphuric acid is added in such quantity as to represent 5 per cent. of the mixture. Distil until the distillate is no longer rendered cloudy by addition of bromine-water. The distillate is filtered, if necessary, and colored a permanent light yellow with bromine-water. The mixture is allowed to remain two or three days at a moderate temperature. A precipitate of tribromophenol ($C_6H_2Br_3OH$) forms and is collected on a weighed filter, washed with water, and dried in an exsiccator over sulphuric acid to constant weight; 100 parts of tribromophenol correspond to 28.4 parts phenol.

INDOXYL-POTASSIUM SULPHATE ($C_8H_6NO.SO_3K$).

(INDICAN ?)

Indole (C_8H_7N), the basis of the above substance, is formed in the intestines; indoxyl, as a radicle thereof, has the formula C_8H_6NO, which, united with SO_3K, forms the indoxyl-sulphate of potassium of the urine. It occurs in white tablets and plates, soluble in water, but sparingly soluble in alcohol. By oxidation indigo blue is formed therefrom. Indoxyl-potassium sulphate has received the erroneous name of indican, under the mistaken belief that it is identical with vegetable indican. But the latter substance is a glucoside, and only resembles the former in the fact that one of its decompositional products is indigo blue.

The blue, green, and some red urines met with in disease probably owe their colors to this salt in different stages of oxidation. It is excreted in excess on an exclusive meat diet, or the ingestion of indole. Clinically an increased excretion of this substance by the kidneys is observed in Addison's disease, cholera, carcinoma of the liver, chronic phthisis, central and peripheral diseases of the nervous system, typhoid fever, dysentery, and the stage of reaction in cholera. In obstructive diseases of the small intestine its excretion is enormously increased. In general, the appearance of large quantities of this substance in the urine implies that abundant albuminous putrefaction is progressing in some part of the system. Sometimes, as urine is undergoing decomposition changes, a bluish-red pellicle, consisting of microscopic crystals of indigo blue and red, is seen,—due to decomposition of the indoxyl-sulphate.

Detection.—1. *McMunn's method:* Equal parts of urine and hydrochloric acid with a few drops of nitric acid are boiled together, cooled, and agitated with chloroform. The chloroform is colored violet, and shows an absorption band, before *D*, due to indigo blue, and another after *D*, due to indigo red.

2. *Jaffe's method:* Mix 10 cubic centimetres of strong hydrochloric acid with an equal volume of urine in the test-tube, and while shaking add drop by drop a perfectly-fresh saturated solution of chloride of lime, or chlorine-water, until the deepest attainable blue color is reached. The mixture should next be agitated with chloroform, which readily takes up the indigo and holds it in solution, and the quantity present may be approximately estimated according to the depth of the color.

If the urine contain albumin, it should be removed before applying these tests, otherwise the blue color often arising from the mixture of hydrochloric acid and albumin after standing may prove misleading.

3. Pour 4 cubic centimetres of hydrochloric acid into a small flask, and while stirring add from 10 to 20 drops of urine. If the proportion of indigo be about normal, the resulting color

will be rather light yellow; if in excess, the acid will turn violet or blue,—the more intense will be the color in proportion to the quantity present. If no coloration appear after waiting a minute or two, there is no excess, however deep a color may subsequently appear.

In addition to those considered, the urine contains three other ethereal sulphates,—viz., creosol-potassium sulphate, catechol-potassium sulphate, and skatoxyl-potassium sulphate. These for the most part are present in minute amounts, and possess the same significance as those considered.

URINARY PIGMENTS.

NORMAL UROBILIN.

Urobilin is the chief coloring agent of normal urine, although it is not the exclusive one, as shown by spectroscopic analysis. Normal urobilin is a dark-brown, amorphous, rather resinous substance, sparingly soluble in water, but readily dissolved by alcohol, ether, chloroform, acids, and acidulated water, as well as by solutions of sodium, potassium, or ammonium hydroxid.

The origin of urobilin is still the subject of some difference of opinion. Formerly, it was believed that bilirubin, entering the intestines with the bile, was acted upon by nascent hydrogen resulting from putrefaction, and as a result it constituted a reduction product, which Maly considered identical with hydrobilirubin. It was also supposed that the pigment of the fæces was partly absorbed, carried to the kidneys, and there excreted. Hydrobilirubin, stercobilin, and urobilin were considered identical, but spectroscopic examinations prove them to be different.

McMunn regards the formation of urobilin as the result of oxidation processes by means of nascent oxygen, either in the intestines or elsewhere, rather than due to reduction processes. He bases this view principally on the fact that, by the action of hydrogen peroxide on acid hæmatin, he is able to prepare an artificial product, which shows the same spectroscopic appearances as normal urobilin. The question, then, whether stercobilin and urobilin are products of reduction or oxidation is still unsettled. It is important to remember, however, that urobilin may originate either from bile-pigment or from blood-pigment.

Certain facts point to the inference that stercobilin and urobilin originate—at least, to a limited extent—independently. Thus: 1. In animals with biliary fistula, while no bile enters the intestine, yet the urine still contains urobilin. 2. In Copeman and Winston's case of biliary fistula, in which no bile had entered the intestine, the fæces were uncolored by stercobilin, yet the urine still contained urobilin. 3. Some cases recorded by Mott would seem to indicate that the formation of urobilin is seated in the liver. When destruction of the red corpuscles is excessive in the portal circulation, the liver contains an excess of iron, and the ferric residue of hæmoglobin occurs as urobilin in the urine abnormally abundant.

Urobilin exists in normal urine in small amount, the quantity being much increased in acute fevers,—four to five or more times. Typhoid and septic fevers, which cause rapid destruction of the blood-corpuscles, markedly increase the excretion of urobilin. On the other hand, there is diminished excretion of urobilin in conditions associated with diminished metamorphosis of red blood-corpuscles, as chlorosis and anæmia, in convalescence from acute diseases, as well as in hysteria and nervous diseases. It is an interesting and highly-important clinical fact that increased excretion of urobilin has been observed in intra-cranial hæmorrhages, hæmorrhagic infarctions, retro-uterine hæmatocele, and extra-uterine pregnancy.

According to the observations of Lawson, the excretion of urinary pigment is much greater in tropical than in temperate climates. Thus, assuming the normal unit to be 4.8 in the average adult in temperate climates, he found in the tropics that it rose to 12 or 14. In pneumonia it has been observed to rise to 16 and 20; in acute rheumatism, from 30 to 32 at the height of the disease; in typhoid fever, from 80 to 100; and in a man who had inhaled arsenated hydrogen, from 600 to 800.

Detection.—Upon rendering the urine alkaline by the addition of ammonium, and, after filtering, adding some chloride-of-zinc solution to the filtrate, a beautiful green fluorescence may be observed by reflected light if urobilin be present. The above solution furthermore exhibits, with the spectroscope, a dark absorption-band between Fraunhofer's lines *b* and *F*.

Uroerythryn.

By some this is considered identical with skatole-pigment, but McMunn claims for it certain characteristic reactions. It is chiefly this pigment which colors the urates a reddish tint, and it may be extracted therefrom by boiling alcohol. This solution gives two ill-defined bands before *F* in Fraunhofer's scale. In the solid state it becomes green with sodium or potassium hydroxid. The origin of uroerythryn in the economy, as well as its relationship to urobilin, have not been determined.

Urochrom.

This name was first applied by Thudicum to the body which he considered the chief coloring agent in the urine. Urochrom is thought by some to consist of impure urobilin. Certain it is, at least, that urochrom contains much urobilin. Urochrom occurs in yellow scales, which partly dissolve in water, less soluble still in alcohol, but soluble in ether and dilute mineral acids and alkalies. The aqueous solution becomes dark on standing, finally changing to a red color, becoming turbid, and depositing resinous flocculi. Urochrom is precipitated from its aqueous solution by nitrate of silver as a gelatinous mass soluble in nitric acid; acetate of lead gives a white flocculent precipitate. Mercuric nitrate gives a white precipitate, which, on boiling, becomes a pale flesh-color, the supernatant fluid appearing rose-red. By oxidation there is first formed from urochrom a red substance, which corresponds to uroerythrin, and to which the red urine of disease often owes its color.

Other Organic Constituents of Urine.

Oxalic Acid ($C_2H_2O_4$).—This substance never occurs in the urine in a free state, but always in combination with calcium (oxalate of lime), which is held in solution by the acid sodium phosphate of the urine. It is sometimes absent from the normal urine, though usually present in quantity of about 0.1 gramme for twenty-four hours. When present in excessive quantities in the urine it is precipitated in the form of oxalate-of-calcium crystals. These are distinguished by their form,—quadratic octahedra, with a short principal axis,—often termed "envelope crystals." Occasionally dumb-bell forms are seen. The origin of oxalic acid in the organism is undetermined; but a close relationship evidently exists between it and uric acid.

Succinic Acid ($C_4H_6O_4$) is the third of the series of acids of which oxalic acid is the primary. Succinic acid has occasionally been met with in the urine, especially after the ingestion of asparagus and asparagin.

Lactic Acid ($C_3H_6O_3$).—It is doubtful if lactic acid be present in normal urine, but it has been found combined with bases after physiological disturbances and severe muscular labor. In such cases it occurs as sarcolactic acid. It has been found in trichinosis, acute yellow atrophy of the liver, cirrhosis of the liver, diabetes, phosphorus poisoning, rickets, leucocythæmia, osteomalachia, and in animals after extirpation of the liver.

Fatty Acids.—These are present in normal urine, though in mere traces,—0.008 gramme per day. They consist of formic, acetic, butyric, and propionic acids. The excretion of fatty acids by the kidneys is increased during the process of ammoniacal fermentation. Certain febrile diseases cause an increase of these bodies in the urine to 0.06 gramme, and in certain diseases of the liver the increase reaches from 0.6 to 1 gramme per day. These acids apparently exist in the urine in a free state.

Glycero-phosphoric Acid ($C_3H_9PO_6$) occurs in faint traces in normal urine, about 15 milligrammes per litre. It is said to be increased in nervous disorders and after chloroform narcosis.

CARBOHYDRATES.—Much discussion has taken place over the question as to whether grape-sugar is a constituent of normal urine. One difficulty in determining this point is the fact that the urine contains a number of substances which reduce alkaline solutions of cupric hydrate, the chief of these being uric acid, hippuric acid, pyrocatechin, glycuronic acid, and creatinin. Abeles showed, however, that none of these substances undergo alcoholic fermentation with yeast, while this does occur with the reducing substance of normal urine. Wedenski, by shaking a large quantity of normal urine with benzoic chloride, obtained insoluble benzoyl compounds of carbohydrates, which give all the reactions of grape-sugar. It may therefore be considered as conclusive, as Brucke first affirmed, that minute quantities of sugar exist in normal urine.

Animal Gum.—This constitutes a product of mucin, and was first found in the urine by Landwher; also in saliva, the synovia, in colloid cysts, in chondrin, and in connective tissue. It forms an opalescent solution with water; gives a sticky precipitate with copper sulphate, and also with ferric chloride. It is precipitated by alcohol, and does not reduce alkaline solutions of cupric salts. It yields oxalic acid upon treatment with nitric acid, and lævulic acid after treatment with hydrochloric acid, as does vegetable gum.

Milk-sugar occurs in variable quantities in the urine of nursing mothers and lesions of the mammary glands. Hofmeister precipitated urine with lead acetate and ammonium, filtered, shook the filtrate with silver oxide, filtered, decomposed the filtrate with sulphuretted hydrogen to get rid of the silver, filtered; to the final filtrate barium carbonate was added, and the mixture evaporated to dryness. Alcohol removed milk-sugar from the residue, and characteristic crystals thereof were obtained by evaporating off the alcohol. Kaltenbach proved that this was milk-sugar by further obtaining therefrom galactose and mucic acid.

Inosite.—This substance has been found in normal urine in small quantities by numerous observers. An increased excretion has been noted in Bright's disease and in diabetes. It may be detected as follows: Several litres of urine, feebly acidified, are completely precipitated with acetate of lead and filtered. The filtrate is warmed and precipitated with basic lead acetate. After standing forty-eight hours the precipitate is collected, washed, suspended in water, and treated with a stream of sulphuretted hydrogen; the lead sulphide is filtered off; uric acid separates from the filtrate after a few hours; this is also filtered off. The solution is then evaporated to a syrupy consistence on a water-bath, and absolute alcohol added. The precipitate is dissolved in hot water, and three or four times the volume of 90-per-cent. alcohol added. Ether is cautiously added till a permanent cloud appears; the inosite crystallizes out, and may be collected. It will then give its characteristic tests, as follows: 1. With a few drops of nitric acid on a platinum dish, treated with ammonium and calcium chloride, after evaporating to dryness a bright red or violet color appears. 2. Add a little mercuric nitrate to a solution of inosite, on a porcelain capsule, a yellow precipitate results. On gently heating, this becomes red; on cooling, the color vanishes. Proteids, tyrosin, and sugar must be absent.

FERMENTS.—*Pepsin* has been isolated from normal urine by Brucke, Sahli, and others. The morning urine is richest in pepsin. The pepsin of urine forms peptone and all intermediate proteoses from fibrin, the same as does pepsin. *Detection:* Small pieces of fibrin are first soaked in urine until pepsin is absorbed therefrom. If then removed to 0.1 per cent. hydrochloric-acid solution they are rapidly digested. Control experiments, with fibrin not soaked in urine, give negative results.

Diastase.—Holvotschiner has obtained minute quantities of ptyalin or a similar diastatic ferment from urine.

Rennet.—Helwes and Holvotschiner have both obtained from urine traces of a ferment which curdles milk.

Trypsin.—This ferment is doubtless absent from normal urine. Sahli alone, of all investigators, claims to have found it; but his results are considered as due to non-putrefaction in his experiments.

MUCIN.—This is the chief constituent of the mucus of normal urine, derived from the muciparous glands of the urinary passages, but not from the kidneys. In normal urine, mucin occurs in small amount; but in catarrhal diseases of the urinary tract it is increased, often in abundance. In appearance it is viscid, slimy, and tenacious.

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Detection: 1. Mucin is precipitated from its solutions by vegetable acids, the precipitate being insoluble in excess of the acid. 2. Add to one volume of urine three volumes of strong alcohol and let stand for several hours. Filter and wash the precipitate with alcohol, and treat with warm water. The filtrate containing the mucin is then acidified with acetic acid, and if turbidity results it is due to mucin.

INORGANIC CONSTITUENTS.

The inorganic constituents of the urine comprise chiefly the chlorides, carbonates, sulphates, and phosphates. These occur in combination with potassium, ammonium, calcium, and magnesium. Small quantities of fluorine, silic acid, and iron are also present; and free gases, including carbonic acid, nitrogen, and traces of oxygen. The total amount of these salts in the urine varies from 9 to 25 grammes per day. They are derived from (*a*) the food ingested and (*b*) from the metabolic processes or tissue-changes; the latter more especially with regard to the sulphates and phosphates. The salts of the blood and those of the urine are very similar, save that the blood contains but traces of sulphates, while the urine is rich in these salts.

The sulphates are derived chiefly from the changes occurring in the proteids of the body; the nitrogenous elements of the proteids being excreted as uric acid and urea, while the sulphur becomes oxidized, forming sulphuric acid, which appears in the urine mostly in combination with metallic bases, but also, to some extent, in ethereal combinations with organic radicles, making up the ethereal sulphates just considered.

CHLORIDES.

The chlorides of the urine consist chiefly of chloride of sodium with a small amount of chloride of potassium and ammonium. The amount of chlorides excreted by the kidneys in the healthy adult averages from about 10 to 16 grammes in twenty-four hours,—6 to 10 grammes of chlorine. The chlorides, therefore, next to urea, constitute the principal solid constituent of the urine. Chlorine is very widely distributed throughout the organism, nearly always in combination with sodium, potassium, ammonium, and magnesium. As chloride of sodium it is excreted with the perspiration, saliva, bile, fæces, and urine.

In health the excretion of the chlorides by the kidneys varies in amount according to the quality and quantity of food ingested. Thus, upon a liberal salt diet they are largely increased; the output representing very closely the amount of chloride of sodium taken in. With active exercise there is also increased excretion of chlorides by the kidneys, while, on the other hand, during repose of the body they are diminished.

Clinically the excretion of chlorides with the urine is diminished in all acute febrile conditions, and especially when attended by serous exudations. As a general rule, in such cases there is a steady decrease until the crisis of the disease is reached, after which they gradually increase. A continued increase of chlorides in the urine in febrile states may, therefore, be accepted as an evidence of improvement. In pneumonia the chlorides may disappear from the urine, and their absence, under such circumstances, always indicates a serious condition of the patient. In chronic conditions associated with impaired digestion and dropsy the chlorides are diminished. In the latter case much of the chlorides become stored up in the dropsical fluid in the serous cavities and cellular tissues. The chlorides are excreted by the kidneys in excess in diabetes insipidus and in the declining stages of dropsy after the establishment of diuresis.

Detection.—1. The urine is treated with nitric acid and a solution of nitrate of silver added. A caseous precipitate soluble in ammonium, insoluble in nitric acid, shows the presence of chlorides.

2. The above test may be made available for approximative estimation as follows: A standard solution of nitrate of silver, 1 to 8 (1 drachm to the ounce), is first prepared. Take a glass half full of urine, and add a few drops of nitric acid; then add one or two drops of the standard solution of silver nitrate, and note the changes. If a white, flaky precipitate occur, quickly sinking to the bottom of the glass without diffusing through the urine, the chlorides are undiminished. If a simple cloudiness appear, readily diffusing throughout the urine without the appearance of curdy flakes, the chlorides are diminished to 0.1 per cent., the normal being 0.5 to 1 per cent. Should no precipitate whatever occur, the chlorides are absent. This method,

proposed by Ultzmann, is not satisfactory, and the author prefers his centrifugal method. (See "Centrifugal Analysis.")

Determination.—*Mohr's Method:* Prepare the following solutions: 1. Standard nitrate-of-silver solution: Dissolve 29.075 grammes of fused nitrate of silver in 1000 cubic centimetres (1 litre) of distilled water; 1 cubic centimetre of this solution is equal to 0.01 gramme of sodium chloride. 2. A saturated aqueous solution of neutral potassium chromate.

Process.—Take 10 cubic centimetres of urine; dilute with 100 cubic centimetres of distilled water; add to this a few drops of the potassium-chromate solution. Drop into this mixture from a burette the standard nitrate-of-silver solution; the chlorine combines with the silver to form silver chloride in the form of white precipitate. When all the chlorides are thus precipitated, silver chromate (red) appears, though not while any chloride remains in solution. The silver nitrate must, therefore, be added until a pink tinge appears. Read off the quantity of standard solution of silver used, and calculate therefrom the quantity of chlorides in the 10 cubic centimetres of urine tested, and from this the percentage.

Corrections.—1. A high-colored urine may cause difficulty in determining the appearance of the pink tinge. This may be obviated by diluting the urine to a normal color. 2. One cubic centimetre should be subtracted from the total number of cubic centimetres of the silver-nitrate solution employed, as the urine contains small quantities of certain compounds more easily precipitable than the chromate. 3. To obviate such errors the following modification of the test as advised by Sutton is employed: Ten cubic centimetres of urine are measured into a thin porcelain dish and 1 gramme of pure ammonium nitrate added; the whole is then evaporated to dryness, and gradually heated over a small spirit-lamp to low redness till all vapors are dissipated and the residue becomes white. It is then dissolved in a small quantity of water, and the carbonates produced by combustion of the organic matter neutralized by dilute acetic acid; a few grains of pure carbonate of lime are added to remove all free acid, and one or two drops of potassium chromate. The mixture is then titrated with deci-normal silver solution (16.966 grammes silver nitrate per litre) until the pink color appears. Each cubic centimetre of silver solution represents 0.005837 gramme of salt; consequently, if 12.5 cubic centimetres have been used, the weight of salt in 10 cubic centimetres of urine is 0.07296 gramme, or 0.7296 per cent. If 5.9 cubic centimetres of urine are taken for titration, the number of cubic centimetres of silver solution used will represent the number of parts of salt per 1000 parts of urine.

Liebig's method consists in estimating the chlorine with mercuric nitrate, but it sometimes fails unless very accurately manipulated, and, moreover, it often gives erroneous results, and therefore it is only referred to here.

Volhard and Falch Method.—This method depends upon the action of soluble sulphocyanides with solutions of silver and ferric salts. Soluble sulphocyanides produce in silver solutions a white precipitate similar to silver chloride, which is insoluble in dilute nitric acid. A like precipitate of sulphocyanide of silver with a solution of nitrate of silver is given by the blood-red solution of sulphocyanide of iron, and the color of the latter at last completely disappears. If, therefore, a solution of sulphocyanide of potassium be added to an acid solution of nitrate of silver, to which a little ferric sulphate has been added, every drop of the sulphocyanide solution at first produces a blood-red cloud, which, however, quickly disappears again on stirring, while the fluid becomes milk-white. It is not until all the silver is precipitated that the red color of the sulphocyanide of iron remains permanent, and the end of the process is reached. The reaction is one of great delicacy; so that it is equally sensitive as Mohr's reaction, while it has the advantage over the latter that titration can be conducted in acid urine.

Solutions Required.—1. *Standard silver solution* is made by dissolving 29.075 grammes of pure silver nitrate in water and diluting to 1 litre. Each cubic centimetre corresponds to 10 milligrammes of chloride of sodium or 6.065 milligrammes of chlorine.

2. *Solution of Ferric Oxide.*—A cold saturated solution of crystallized ferric alum, free from chlorine, or a solution of ferric sulphate, which contains 50 grammes of iron oxide to the litre.

3. *Standard Sulphocyanide-of-Potassium Solution.*—Since sulphocyanide of potassium cannot be readily weighed with accuracy, 10 grammes are dissolved in a litre of water, and this solution is standardized by silver solution. Thus 10 cubic centimetres of the silver solution are measured off, 5 cubic centimetres of the iron solution are added, and then pure nitric acid is added drop by drop until the mixture is colorless. If the sulphocyanide-of-potassium solution be then allowed to flow into it from a burette, each drop at first gives a blood-red color, which at once disappears on stirring. When all of the silver is precipitated as sulphocyanide of silver, the next drop of the sulphocyanide-of-potassium solution gives a permanent red color to the fluid, indicating the end of the reaction. If, for example, to 10 cubic centimetres of the silver solution 9.6 cubic centimetres of the sulphocyanide-of-potassium solution have been used before the red color is permanent, 960 cubic centimetres are measured off, and this is diluted with 40 cubic centimetres of water to make a litre. Both solutions must now be equivalent, which is to be determined by titration.

Analysis.—Five or 10 cubic centimetres of the urine, after the addition of 1 or 2 grammes of nitrate of potassium free from chlorine, are evaporated to dryness on a water-bath. The residue is then heated over a free flame, at first gently, afterward strongly, and a white, fused residue remains. Since the nitrous acid formed in this process prevents the end reaction, the fused saline mass is dissolved in water, acidulated with nitric acid, and then the chlorine is precipitated with an excess of the standard silver solution. After this mixture has been warmed on a water-bath for a time to completely remove the nitrous acid, it is allowed to cool; 5 cubic centimetres of the iron solution are added, and then the sulphocyanide-of-potassium solution, equivalent in strength to the silver solution, is added while constantly stirring until the excess of the silver added is precipitated, which is known by the permanent red color of the mixture. The difference, then, between the number of cubic centimetres of the silver and sulphocyanide solutions corresponds to the chlorine contained in the urine. If, for instance, at first 12 cubic centimetres of the silver solution were added to 10 cubic centimetres of urine, and 4 cubic centimetres of the sulphocyanide solution were required to titrate back the excess, the amount of chlorine in the urine corresponded to $12 - 4 = 8$ cubic centimetres of the silver soluion $= 8.0$ grammes of sodium chloride or 4.852 grammes of chlorine in the litre of urine.

PHOSPHATES.

The quantity of phosphoric acid excreted by the kidneys in the healthy adult ranges from 2.3 to 3.5 grammes in twenty-four hours, the average being about 2.8 grammes. Ordinary phosphoric acid (H_3PO_4) is tribasic, containing 3 atoms of hydrogen, which may be replaced by a metal. In the urine phosphoric acid occurs in combination, in part with the alkaline earths—*earthy phosphates*, and in part with the alkalies—*alkaline phosphates*. *The earthy phosphates* are insoluble in water, but soluble in acids, and consist of phosphates of calcium and magnesium. The calcium phosphates are most abundant; those of potassium scanty. They exist in the urine in quantity of about 1 to 1.5 grammes in twenty-four hours' excretion,—the relative proportion being calcium phosphate about 33, and magnesium phosphate about 67. In acid urine the earthy phosphates are in solution, while in alkaline urine they are precipitated and form a sediment more marked if heat be applied. If, therefore, an alkaline urine is heated in a test-tube, a precipitate forms, which may be mistaken for albumin. It may, however, be distinguished from the albuminous reaction by slight acidification, which readily dissolves the earthy phosphates. This is a frequent source of error in testing for albumin in the urine by means of heat. If the acid magnesium phosphate be acted upon by ammonium the ammonio-magnesium phosphate is formed,—*triple phosphate*. This appears in the urine as fern-leaf or snow-flake crystals, or, after long standing, in the form of prismatic or "coffin-lid" shaped crystals. If urine decompose in the bladder through retention and consequent fermentative changes, ammonium is liberated from the urea, and the free ammonium unites with the acid magnesium phosphates to form the triple phosphatic crystals so characteristic of chronic cystitis.

The alkaline phosphates of the urine consist of the acid phosphate of sodium and the phosphate of potassium, that of sodium being most abundant and the potassium phosphate scanty. These (unlike the earthy phosphates) are readily soluble in water and alkaline fluids. The alkaline phosphates form the chief bulk of the phosphates of the urine, ranging from 2.0 to 4.0 grammes in twenty-four hours. As already noted, the acidity of normal urine depends upon its contained acid sodium phosphate, and not upon the presence of a free acid.

In the blood the alkaline phosphates exist as neutral sodium and potassium phosphates; but, as Ralfe has shown,[1] these are changed into acid salts through a decomposition effected by the act of secretion, in which the bicarbonates and neutral phosphates in the blood are changed into carbonates and acid phosphates, respectively. The acid salts, in obedience to the law of diffusion, pass out in the urine, whilst the carbonates remain in the circulation. The excretion of the alkaline phosphates by the kidneys varies in health according to the quality of food ingested, being in excess upon an animal diet.

The phosphoric acid of the urine is derived in part from the food and in part from the decomposition of lecithin and nuclein. The excretion of phosphoric acid by the kidneys varies with the amount of food taken; after the midday meal, especially if much meat be eaten, it rises, and reaches its maximum in the evening; it falls during the night, reaching its minimum about midday.

Clinically, the excretion of phosphoric acid by the kidneys is diminished in gout, in most acute diseases, in kidney lesions, in the intervals of intermittent fever, and during pregnancy. The author regards the diminution of phosphoric-acid excretion by the kidneys almost as constant a feature of the urine in Bright's disease and allied lesions of the kidneys as the presence in the urine of albumin.

An increased excretion of earthy phosphates accompanies diffuse diseases of the bones,—osteomalacia, rickets, etc.; also in diffuse periostitis and diseases of the nerve-centres.

A condition of so-called *phosphatic diabetes* has been described by Tessier and confirmed by Ralfe and others, in which there is a continued excessive excretion of phosphates by the kidneys, attended by symptoms somewhat like diabetes,—loss of flesh; aching pains in the lower back and pelvic region; dry, harsh skin; tendency to boils, with morbid appetite, etc.

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[1] Lancet, July, 1874.

Detection.—1. The *earthy phosphates* may be detected by rendering the urine strongly alkaline with sodium, potassium, or ammonium, and gently heating, which cause their precipitation in the form of a whitish cloud, that shortly after settles to the bottom of the test-glass. The precipitate is dissolved upon the addition of acetic acid.

2. Ultzmann suggests an approximative method with this test, as follows: A test-tube 2 centimetres (0.787 inch) wide is filled with the urine to the depth of 5.33 centimetres (2.997 inches), to which is added a few drops of caustic ammonium or potassium solution, and warmed over a spirit-lamp until the earthy phosphates separate. After standing fifteen minutes the depth of the sediment is measured. If the layer be 1 centimetre (0.3937 inch) high, the earthy phosphates are present in normal amount; if 2 or 3 centimetres in depth they are increased; but if the sediment be only a line or so in depth, they are diminished.

The Alkaline Phosphates.—1. First remove the earthy phosphates by precipitation with potassium or ammonium and filter them off. Next add to the urine one-third of its volume of magnesium fluid.[1] The alkaline phosphates are all precipitated in the form of a snowy deposit.

2. The above test may be made useful for approximative estimation, as Ultzmann suggests, in the following manner: To 10 cubic centimetres of the urine add a third part (say, 3 cubic centimetres) of magnesium mixture. There is formed a precipitate of crystalline ammonium-magnesium phosphate, with which comes down an amorphous mass of calcium phosphates. If there ensue through the entire fluid a milky turbidity, the alkaline phosphates are in normal amount; if we have a copious precipitate, which gives the fluid the appearance of cream, then there is great increase; if the fluid remain transparent, or only slight turbidity ensue, we have a decrease of the alkaline phosphates.

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[1] *Magnesium fluid* contains, of magnesium sulphate and ammonium chloride, each 1 part; distilled water, 8 parts; and pure liquor ammonium, 1 part.

Determination of Total Phosphoric Acid.—The following solutions are necessary:—

1. A standard solution of uranium nitrate is prepared, consisting of 20.3 grammes pure uranic oxide in 1000 cubic centimetres of distilled water; 1 cubic centimetre corresponds to 5 milligrammes of phosphoric acid.

2. Sodium-acetate solution: 100 grammes of sodium acetate are dissolved in 900 cubic centimetres of distilled water, and to this 100 cubic centimetres of acetic acid are added.

3. Saturated solution of potassium ferrocyanide.

Analysis.—Fifty cubic centimetres of the urine are poured into a beaker, and 5 cubic centimetres of sodium-acetate solution are added. The mixture is warmed over a water-bath and the uranium solution added, drop by drop, as long as a precipitate falls. If this be not easily recognized, the mixture should be stirred, a drop placed upon a porcelain plate, and a drop of potassium ferrocyanide added. If a reddish-brown color do not appear at the line of contact, the addition of uranium solution should be continued, the beaker-glass being again warmed. The limit of reaction occurs when all the phosphoric acid has been precipitated by the uranium solution. After this is reached, the next drop of uranium solution, finding no phosphoric acid, forms a reddish-brown precipitate with potassium-ferrocyanide solution. The quantity of uranium solution used is next read off, each cubic centimetre being equal to 5 milligrammes phosphoric acid, from which can be readily calculated the percentage amount in the urine.

Estimation of Phosphoric Acid Combined with Lime and Magnesium.—To determine the phosphoric acid in combination with the earths, 200 cubic centimetres of urine are precipitated with ammonium, collected after twelve hours on a filter, and washed with ammonium-water (1 to 3). The filter is then pierced at the point, and the precipitate washed down with a stream of water into a beaker, and dissolved while warm with as little acetic acid as possible. Add 5 cubic centimetres of sodium-acetate solution, dilute to 50 cubic centimetres, and proceed as in preceding analysis. The difference between the total amount of phosphoric acid and that in combination with the alkaline earths also represents the quantity combined with the alkalies,—alkaline phosphates.

SULPHATES.

The sulphates in the urine are of two kinds (1) ordinary neutral sulphates of sodium and potassium, and (2) the ethereal sulphates. Since the sodium salts predominate in the economy, the sulphate of sodium occurs in the urine in greater quantity than the potassium sulphate. The quantity of sulphates excreted by the kidneys in the healthy adult varies from 1.5 to 3 grammes per day. The sulphates, being extremely soluble compounds, are, therefore, never met with in the urine in the form of deposits.

An increased excretion of sulphates by the kidneys occurs after the ingestion of sulphuric acid or its salts, upon active exercise, upon an exclusive meat diet, and inhalations of oxygen-gas. Clinically an increase occurs in acute fevers, with increased urea secretion. The most marked increase is noted in meningitis, encephalitis, and rheumatism. In general, it may be accepted that the excretion of urinary sulphates runs parallel in quantity to that of urea.

Detection.—1. To 10 cubic centimetres of urine add a few drops of hydrochloric acid, then add about 3 cubic centimetres of barium-chloride solution; a white, milky precipitate is formed of sulphate of barium.

2. More simply still, to 10 cubic centimetres of urine in a test-tube add one-third the volume of acidulated barium-chloride solution,[1] when a white, milky precipitate at once appears in the presence of sulphates.

3. Approximate estimation may be made by the above as follows: If a simple, opaque, milky turbidity result, the sulphates are present in about the normal amount; if more opaque, possessing the appearance of cream, the sulphates are excessive; if but a light translucent cloudiness result, the sulphates are diminished.

Determination.—(*a*) The volumetric method is conducted by adding to a given volume of urine a standard solution of barium chloride as long as precipitation occurs.

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[1] Baric chloride, 4 parts; acid hydrochloric, 1 part; distilled water, 16 parts.

Solutions Required.—1. A standard chloride-of-barium solution: 30.5 grammes of crystallized barium chloride to 1000 cubic centimetres of distilled water; 1 cubic centimetre of this solution corresponds to 0.01 gramme of sulphuric acid.

2. Solution of potassium sulphate, 20 per cent.

3. Pure hydrochloric acid.

Analysis.—One hundred cubic centimetres of urine are rendered acid by 5 cubic centimetres of hydrochloric acid, and brought to boiling in a flask. The combined sulphates are thus converted into ordinary sulphates, and give a precipitate similarly with barium chloride. The chloride-of-barium solution is allowed to drop into the mixture as long as any precipitate occurs, the mixture being heated before each addition of barium chloride thereto. After adding 5 to 8 cubic centimetres of the standard solution, allow the precipitate to settle; pipette off a few drops of the clear, supernatant fluid into a watch-glass; add to it a few drops of the standard barium solution. If any precipitate occur, return the whole to the flask and add more barium chloride; again allow the precipitate to settle and test as before; continue thus until no more precipitate is formed on the addition of barium-chloride solution.

Excess of barium chloride should be avoided; when only a trace of excess is present, a drop of the clear fluid removed from the flask gives a cloudiness with a drop of potassium-sulphate solution placed on a glass plate over a black ground. If more than a cloudiness appear, too large a quantity of barium chloride has been added, and the analysis must be repeated.

From the quantity of barium chloride used, the percentage of sulphuric acid in the urine is calculated,—1 cubic centimetre of barium-chloride solution corresponding to 0.01 gramme of SO_3.

(*b*) *Gravimetric determination* is best conducted as suggested by Salkowski. This consists in washing the precipitate of barium sulphate obtained by adding barium chloride to a known volume of urine; 100 parts of sulphate of barium correspond with 34.33 parts of sulphuric acid (SO_3).

Analysis.—One hundred cubic centimetres of urine are taken in a beaker; this is acidified with 5 cubic centimetres of hydrochloric acid. Chloride of barium is added till no more precipitation occurs. The precipitate is collected on a small filter of known ash, and washed with hot distilled water till no more barium chloride occurs in the filtrate, *i.e.*, until the filtrate remains clear after the addition of a few drops of hydric sulphate. Then wash with hot alcohol, and afterward with ether. Remove the filter and incinerate with its contents in a platinum crucible. Cool over sulphuric acid in an exsiccator; weigh, and deduct the weight of the crucible and filter ash; the remainder is the weight of barium sulphate formed, from which the SO_3 is readily calculated,—100 parts of barium sulphate corresponding with 34.33 parts of SO_3.

Correction.—As carried out above, a slight error occurs in the analysis from the formation of a small quantity of sulphide of barium. Correct as follows: After the platinum crucible has cooled add a few drops of pure sulphuric acid (H_2SO_4). The sulphide is converted into sulphate. Heat again to redness and drive off the excess of sulphuric acid.

(*c*) Salkowski's method of estimating the *combined sulphuric acid*—*i.e.*, the amount of SO_3 in ethereal sulphates—is as follows: 100 cubic centimetres of urine are mixed with 100 cubic centimetres of an alkaline barium-chloride solution, which is a mixture of two volumes of solution of barium hydrate with one of barium chloride, both saturated in the cold. The mixture is stirred, and after a few minutes filtered; 100 cubic centimetres of the filtrate (= 50 cubic centimetres of the urine) are acidified with 10 cubic centimetres of hydrochloric acid, boiled, kept at 100° C. on a water-bath for an hour, and then allowed to stand till the precipitate has completely settled; if possible, it should be thus left for twenty-four hours. The further treatment of this precipitate (= combined sulphates) is then carried out as in the last case [see (*b*)].

Calculations.—Two hundred and thirty-three parts of barium sulphate correspond to 98 parts of H_2SO_4, 80 parts of SO_3, or 32 parts of S. To calculate the H_2SO_4, multiply the weight of barium sulphate by $\frac{98}{233} = 0.4206$; to calculate the SO_3, multiply by $\frac{80}{233} = 0.34335$; to calculate the S, multiply by $\frac{32}{233} = 0.13734$.

This method of calculation applies to the gravimetric estimation both of total sulphates and of combined sulphates.

(*d*) To obtain the amount of preformed sulphuric acid, subtract the amount of combined SO_3 from the total amount of SO_3. The difference is the preformed SO_3.

Example.—One hundred cubic centimetres of urine gave 0.5 gramme of total barium sulphate; this multiplied by $\frac{80}{233} = 0.171$ gramme = total SO_3. Another 100 cubic centimetres of the same urine gave 0.05 gramme of barium sulphate from ethereal sulphates; this multiplied by $\frac{80}{233} = 0.017$ gramme of combined SO_3. Total SO_3 — combined $SO_3 = 0.171 - 0.071 = 0.157$ gramme of preformed SO_3.

CARBONATES.

Carbonate and bicarbonate of sodium, ammonium, calcium, and magnesium are present in minute quantities in fresh urine of alkaline reaction. The ammonium carbonate may be found in large quantity as a result of alkaline decomposition of the urine. The carbonates of the urine are derived from the food, from lactic, malic, tartaric, succinic, and other vegetable acids in the food. If the urine contain much carbonates when voided it is turbid, or soon becomes so upon standing, and upon sedimentation the precipitate is that of calcium carbonate usually associated with phosphates. Carbonate of lime constitutes the basis of urinary calculus of great rarity in the human subject, very frequent, however, in herbivora.

Detection.—The presence of carbonates in the urine may be revealed by the evolution of colorless gas, upon the addition of acid, and this gas renders baryta-water turbid.

Determination.—The following method of Marchand may be employed for estimating the free carbonic acid of the urine: One hundred cubic centimetres of urine are placed in a glass flask, closely fitted with a doubly-perforated cork. Through one opening a tube is passed, which dips into the urine, and at the other end is connected with a tube containing some quicklime. Through the other opening in the cork one arm of a doubly-bent tube is passed; this arm does not dip into the urine. The other arm is introduced into an empty flask through a tightly-fitting cork. This flask is connected by a similar tube with a second flask filled with clear baryta-water, and this with a third and fourth filled with baryta-water.

The urine is heated to 100° C. over a water-bath; any portions boiling over go into the empty flask. The carbonic acid comes off and forms a white precipitate of barium carbonate in the flasks filled with baryta-water. Air is then drawn through the apparatus, any carbonic acid in the atmosphere being removed by the quicklime. The carbonate of baryta formed is collected on a filter, washed with distilled water, dissolved in hydrochloric acid, precipitated again by sulphuric acid, and weighed as barium sulphate. From the quantity thus obtained the amount of carbonic acid in the urine can be calculated: 196.65 parts of barium carbonate correspond to 232.62 parts of barium sulphate and 44 parts of carbonic acid.

(*b*) The *total carbonic acid* may be similarly estimated after strongly acidifying the urine with hydrochloric acid.

The *combined carbonic acid* is the difference between the total and the free carbonic acid.

OTHER INORGANIC CONSTITUENTS.

Iron occurs in the urine in small quantities, but its combination is yet unknown. Free *ammonia* occurs in traces, greatly increased in putrefactive changes of the urine. *Hydrogen dioxide* was first shown in the urine by Schonben. It exists in small amount, and, so far as known, is without special signification. It is detected by tetra-paper, which, if immersed in its solution, will show the presence of ozone by taking a blue color. 2. Dilute indigo solution is bleached by dioxide of hydrogen in the presence of iron-sulphate solution.

GASES.—The urine contains small quantities of gases. *Carbonic acid*, 4 to 9 volumes free gas; 2 to 5 combined. *Oxygen*, 0.2 to 0.6 volume; and *nitrogen*, 0.7 to 0.8 volume. The gases of the urine may be withdrawn by the air-pump.

CENTRIFUGAL ANALYSIS.

The chemical constituents of the urine, both normal and abnormal, may be estimated by the centrifugal method, and very excellent, as well as rapid, results may thus be obtained. The method followed by the author consists in throwing out of solution the chemical constituents of the urine desired to measure, and estimating the quantity of the insoluble precipitates in bulk percentage. For this purpose the author has devised a set of percentage tubes, which will be found convenient for estimating not only the chemical constituents of normal urine, but also such products of abnormal urine as pus, albumin, etc. These percentage tubes—shown in the figure—are graduated in tenths of a cubic centimetre up to 10 cubic centimetres. The lower portion of the tubes being drawn out in conical form, fractions of the first three cubic centimetres may be more accurately read and measured. Above the graduated scale the tubes possess sufficient capacity for the reception of the reagents ordinarily required to precipitate the urinary constituents to be estimated.[1] The following is the author's method of conducting centrifugal estimations of some of the inorganic constituents of the urine:—

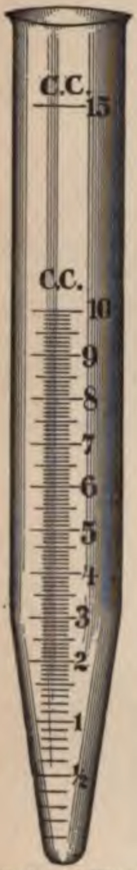

FIG. 7.—AUTHOR'S PERCENTAGE TUBE.

Chlorides.—The percentage tubes are filled to the 10-cubic-centimetre mark with the urine to be tested; a few drops of nitric acid are added to prevent precipitation of the phosphates, and then the tubes are filled to the 15-cubic-centimetre mark with the standard nitrate-of-silver solution (ʒj to ℥j). The tubes are next closed and inverted several times, until the urine and the reagents are thoroughly mingled. The tubes are next placed in the centrifuge and revolved until the sediment is thoroughly packed, when the quantity in bulk percentage may be read off from the graduated scale on the sides of the tubes. From a considerable number of observations the author finds that the bulk percentage of chlorides in normal urine thus obtained ranges from 16 to 18 per cent. Variations from the normal range are quickly indicated, and the degree of variation is definitely measured.

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[1] Eimer & Amend, of 205 and 211 Third Avenue, New York, manufacture and supply the author's percentage tubes for centrifugal analysis.

Phosphates.—The gross quantity of the urinary phosphates are readily determined by the centrifugal method in a similar manner. Thus, the percentage tubes are filled to the 10-cubic-centimetre mark with the urine to be tested, and then the magnesium mixture[1] is added to the 15-cubic-centimetre mark. The tubes are closed and inverted several times, until the urine and reagents are thoroughly mingled. The tubes are then placed in the centrifuge and revolved until precipitation is complete, when the bulk percentage may be read off from the scale.

The chlorides and phosphates precipitated as just described form comparatively heavy sediments, which are deposited by the centrifuge in about one minute. In order, however, to insure uniform results, it is found best to leave the tubes in the centrifuge for three minutes, when the sediments will be found to have packed so solidly that only long-continued revolutions cause further changes in the reading. With the author's electric centrifuge it is advised to revolve the tubes uniformly three minutes, at *moderate speed*, before reading the quantity of chlorides and phosphates. One thousand revolutions per minute, continued for three minutes, give the author's standard results for chlorides, phosphates, and sulphates.

The bulk percentage of total phosphates in normal urine determined as just described will be found to range from 8 to 12 per cent. It may be observed that frequent and wide variations in the amount of urinary phosphates are more common than with any other urinary constituents. Quantitative centrifugal analysis can only be carried out satisfactorily with the electric centrifuge, because hand power cannot give the same uniform and definite rates of speed as electric power.

Sulphates.—These are estimated as insoluble salts of barium, as follows: The percentage tubes are filled to the 10-cubic-centimetre mark with the urine to be tested; the acid barium-chloride mixture is next added to the 15-cubic-centimetre mark;[1] the tubes are then inverted a number of times, until the urine and reagents are mingled. The tubes are then placed in the centrifuge and revolved for three minutes, when the bulk percentage of total sulphates may be read off, the range of which in normal urine will be found about 1 per cent. The rule followed by the author with his electric centrifuge is as follows: *The chlorides, phosphates, and sulphates are sedimented in the percentage tubes by continued revolutions at moderate speed for three (3) minutes.*

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[1] The magnesium mixture consists of ammonium chloride and magnesium sulphate, āā 1 part; distilled water, 8 parts; and liquor ammonia, 1 part.

The term *moderate speed*, wherever applied to the author's centrifuge, means 1000 revolutions per minute.

The author has found this method to give excellent approximate results for practical work, and the advantages of the method are that it can be carried out very rapidly and the variations from the normal standard are definitely measured. Centrifugal analysis may be extended to practically include all urinary constituents. Analysis for chlorides, phosphates, and sulphates are here described, both to illustrate the method and on account of the great practical value of being able so readily to approximately estimate these highly-important constituents. The author hopes soon to furnish methods and standards for centrifugal estimation of most, if not all, the remaining constituents of the urine.

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[1] The acid barium-chloride solution is composed of 4 parts baric chloride, 1 part hydrochloric acid, and 16 parts distilled water.

SECTION III.

ABNORMAL URINE.

PROTEIDS.

THE four proteids of the blood—viz., serum-albumin, serum-globulin, fibrin, and hæmoglobin—are met with in the urine in various pathological conditions of the kidneys, the blood, or the system at large. Other proteids are sometimes met with in the urine which do not exist in the blood, such as egg-albumen upon the liberal ingestion of eggs as food, and, under certain conditions, also peptone. Finally, certain proteoses are met with in the urine in pathological conditions, the more prominent of which are pro-albumose, deutero-albumose, and hetero-albumose.

ALBUMINURIA.

The chief clinical interest with regard to proteids in the urine will probably always centre about serum-albumin. While albumin is doubtless the most common of all the constituents of morbid urine, it still remains a debated question if it be present in the urine in health. No doubts can further exist that the urine occasionally contains a variable—usually small—but distinct amount of albumin when the kidneys present no appreciable alterations of structure; but, as will be shown, albuminuria often arises from causes aside from the kidneys themselves. Albuminuria, therefore, cannot be proved to be a condition of health, so long as the kidneys alone are considered; yet, the absence of renal lesions would seem to be the chief, if not indeed the only, condition sought to be established by many advocates of a so-called physiological albuminuria.

Albumin belongs to the class of colloids which do not crystallize, and under ordinary conditions do not penetrate animal membranes; but alterations from the normal conditions, as in the integrity of the basement membrane, in the quality of the albumin itself, or in the pressure to which they are both subjected, may result in transudation. It is altogether probable that most forms of albuminuria are referable to causes corresponding to one or more of the above-named conditions. In other words, albuminuria may be due (1) to changes in the kidneys themselves, which impair the integrity of the structures between the vessels and the excretory channels of the organs; (2) alterations in the quality of the blood which render its serum-albumin more diffusible; (3) alterations in the degree of blood-pressure. Albuminuria may depend upon one or, indeed, all three of the above conditions.

Clinical Significance.—1. The more common form of albuminuria, as well as the most serious in its clinical significance, is that depending upon pathological conditions of the kidneys. The most frequent of these are inflammatory and degenerative changes in the renal structure, and include the whole class of disorders commonly grouped together under the term of Bright's disease.

It is impossible *always* to estimate the gravity or progress of renal changes by the quantity of albumin present in the urine. Sometimes, however, as in acute inflammatory conditions, when the amount of albumin ranges high,—1 per cent. by actual weight or more,—the quantity may be taken as a rough gauge of the extent of the lesions as well as the progress of the same from day to day. The same may be said of certain degenerative changes in the kidneys, notably of amyloid disease. This, however, by no means applies to all diseases of the kidneys, for, indeed, in certain renal diseases of the most serious character,—*interstitial nephritis*,—not only is the quantity of albumin in the urine usually small, but it is often temporarily, and even occasionally, absent throughout. The quantity of albumin in the urine, therefore, is not a safe guide as to the gravity of the situation in diseases of the kidneys, especially in cases attended by moderate or even very slight grades of albuminuria.

2. The second class of albuminurias depend upon changes in the constitution of the blood, which so alters the diffusibility of its albumin as to permit it to pass into the renal tubules. The hæmotogenic causes of albuminuria have been most ably expounded by Semola, and, although he probably claims too wide a range for these causes, there remains no just reason to doubt

their existence. We often meet with such albuminuria in anæmia, and in strumous and enfeebled individuals, when no lesions of the kidneys can be made out. The effect of certain poisons upon the blood probably so alters that fluid as to permit of transudation of its albumin into the renal tubules. The effects, also, of some infectious fevers—micro-organisms in the blood—no doubt seriously alters the constitution of the circulating fluid, so that transudation of albumin is the rule, while the kidneys do not always become damaged.

3. The third form, disturbances of the circulation, may bring about albuminuria without inducing structural changes in the kidneys, provided they be not too long continued. Circulatory disturbances, in order to induce albuminuria, must include the renal vessels. In nature they must consist of acceleration of the arterial current or slowing of the venous current, in either case resulting in increased blood-pressure. Probably this cause is responsible for the majority of that large class of cases of so-called "*physiological* or *functional albuminurias.*" This is most marked upon prolonged or fatiguing muscular exercise. Leube found albumin in the urine in 16 per cent. of soldiers after prolonged march, and Chateaubourg gives the percentage as even higher. A similar result sometimes occurs after the application of cold to the surface of the body; the blood being driven to the interior, the renal vessels become overfilled and albuminuria often results. Again, in some derangements of the nervous system, which interfere with the vasomotor-nerve regulation of the renal vessels, temporary albuminuria is not an uncommon result. Albuminuria from increased blood-pressure is readily demonstrable by experimentation in the following ways: 1. By pressure upon the renal veins. 2. Ligature of the aorta below one kidney, and extirpation of the other. 3. Compression of the trachea. The quantity of albumin in the urine from disturbances of the circulation is for the most part small. It may be but temporarily present, or it may become a permanent condition, depending upon the continuance of the cause. Thus we may have temporary albuminuria after a seizure of epilepsy which soon after the attack subsides, or when depending upon organic disease of the heart it becomes permanent.

Finally, albuminuria often owes its origin to two or even all three of the causes just considered. In fevers, for instance, all the described causes of albuminuria are sometimes present. We have, for instance, accompanying changes in blood-pressure, and when long continued the febrile state is apt to induce structural changes in the renal epithelium, while profound changes in the constitution of the blood are often induced by fevers, more especially the acute infectious ones, which without doubt are the active cause of albuminuria.

It remains to consider the significance of a form of albuminuria which is often intermittent in character, to which Pavy's "*Cyclic Albuminuria*" and Moxon's "*Albuminuria of Adolescence*" doubtless belong. In a large percentage of these cases the albuminuria is intermittent; if not, usually it is remittent; the intermission or remission occurring during rest, as at night. On rising in the morning the urine is often free from albumin, but soon after rising, and especially upon exercising, the urine contains albumin, which may or may not wear away toward evening. A large percentage of these cases is observed in youths and young adults.

In another class of these cases the albuminuria is more constant, and if an intermission occur it is usually measured by weeks or months instead of hours. In these cases the age of the patient is less constant, although the albuminuria is still most common before middle age.

For the most part all these cases possess certain features in common: 1. The quantity of albumin in the urine is small, usually ranging from one-half to one-tenth or two-tenths of one per cent. 2. The urine either contains no renal casts or very few perfectly hyaline ones. 3. The specific gravity of the urine is somewhat above the normal standard,—1024 to 1030. 4. Evidences of cardiac and general vascular changes of a permanent nature are absent. 5. Close observation will usually reveal evidence of some local or general impairment of the functions, as measured by the standard of vigorous health.

The causes of this group of albuminurias are identical with those already considered, only operating perhaps in milder degrees. To changes in the renal structures, alterations in the quality of the blood, or abnormal increase of blood-pressure,—to one or more, or all of these combined, we may with great probability refer every case of albuminuria as to its essential cause or causes.

It will be seen, from the preceding considerations, that albuminuria is a symptom of the most variable clinical significance, and therefore, in itself, should never be accepted as proof of the presence of renal disease. As has been truthfully said, "this was the error of former times." It can only be positively asserted that albuminuria is the result of renal changes when it is accompanied by those products in the urine which are a consequence of renal lesions, such as casts, epithelium, etc. On the other hand, it must be remembered that albumin in notable quantity is not present in healthy urine. On the whole, it will be safer to accept albuminuria as an evidence of an existing abnormal state, the gravity of which must be determined by its accompanying symptoms. The author holds that so-called functional albuminuria forms no exception to the above rule, inasmuch as he has never met with a case of albuminuria in which the patient did not present more or less evidence of departure from the normal balance of perfect health, either local or general.

It is only necessary here to allude to the occurrence of albumin in the urine derived from sources other than the kidneys. Such albuminuria has been variously termed *adventitious*, *false*, or *accidental*. In such cases the urine on leaving the kidneys is perfectly normal; but, meeting with the products of inflammatory changes in the urinary passages,—the renal pelvis, ureters, bladder, or urethra,—it becomes albuminous. As a rule, in such cases, the source of the albumin may be determined by chemical and microscopical investigation, together with local symptoms.

Detection of Albumin in the Urine.—1. *Heat:* Boiling the urine constituted the first test employed to detect albumin, by Contugno (1770). The more common method of application of this test is in conjunction with nitric acid. A test-tube of ordinary size is filled half full of the suspected urine, and heat is applied until boiling occurs throughout the whole. If a precipitate occur, it consists either of albumin or earthy phosphates. A few drops of nitric acid are next added, and if the precipitate remain undissolved it is due to the presence of albumin. If, on the other hand, the precipitate disappear upon the addition of the acid, it consists of the earthy phosphates, and the urine is free from albumin. In testing, the acid should be added in small quantity, at first,—say, 2 to 5 drops,—and the urine should then be re-boiled. If now no precipitate occur, acidulation should be continued until precipitation occur or a limit of acidification be reached of about 15 to 20 drops. Some prefer to reverse this order, and first acidify the urine before applying the heat.

The heat and nitric-acid test is subject to certain errors. Thus, if there be little albumin present and the acid be in excess, the albumin may combine with the acid, forming a soluble acid albumin,—*syntonine*,—which is not precipitated by boiling. If, on the other hand, the acid be insufficient to distinctly acidify the urine, and if the phosphates be in excess, a part only of the basic phosphates may be acidified, while the albumin may combine with the remainder, forming a soluble alkali albuminate, which will not be precipitated by boiling. The heat and acid test throws down albumin, globulin, and mucin, and upon cooling albumose separates, if present. No reaction occurs with peptone, vegetable alkaloids in the urine, or with the urates. If the urine contain the pine acids, as sometimes occurs after the use of cubeb or copaibæ, these may cause slight precipitation by this test, which may be mistaken for albumin. The ready solubility of this precipitate in alcohol distinguishes it from albumin.

Various modifications have been suggested, with the view of avoiding the mucin reaction which sometimes undoubtedly occurs with this test, such as first boiling the urine and then very faintly acidifying with nitric acid, or by employing acetic instead of nitric acid in quantity not to exceed 2 drops. Such modifications, however, are not to be depended upon in eliminating the occasional mucin error, as will appear by a study of the chemistry of mucin reactions.

2. *The Author's Method.*—Have at hand a solution of chloride of sodium (table-salt), prepared by saturation and filtering, so that it is perfectly clear. First raise the specific gravity of the urine about 10 or 15 degrees by the addition of a little of the sodium-chloride solution. Next fill an ordinary test-tube to

about two-thirds with the urine, add 1 or 2 drops of strong acetic acid, and boil the upper inch or so of the urine about half a minute over a spirit-lamp. Examine in a good light, and if albumin be present it will appear in the upper boiled portion of the urine as a more or less pronounced milk-like turbidity, according to the quantity present, the lower or unboiled portion remaining perfectly clear, in strong contrast. This test possesses all the sensitiveness of the heat and acid test for albumin, and avoids the mucin reaction. The author advises the above modification of the heat and acid test when dealing with *minute quantities of albumin;* with *large amounts of albumin* the old method may be followed.

3. *Nitric-Acid Test.*—This test is applied according to Heller's method, as follows: Upon a column of pure nitric acid in a test-tube the suspected urine is gently floated, so that the column of urine and that of acid are about an inch in depth. In order to accomplish the above without mixing the acid and urine, the test-tube should be held in an inclined position and the urine slowly delivered along the inside of the tube, so that the urine may flow gently down and overlay the acid. If albumin be present, an opalescent zone will be observed *at the point of contact* between the acid and the urine, which becomes more or less pronounced according to the quantity of albumin present. If no change be perceptible upon careful examination in a good light, the tube should be set aside and re-examined in half an hour, because, when only a trace of albumin is present, twenty to thirty minutes may elapse before the zone of coagulated albumin becomes visible.

In concentrated urines with this test the acid is apt to precipitate the amorphous urates in the form of a light, rather brownish cloud, which may be taken for albumin. The cloud of precipitated urates, however, does not appear *at the point of contact* between the acid and the urine, but *higher up*, within the urine itself; moreover, it is more diffused than the albuminous zone, and spreads downward through the urine. The precipitated urates disappear upon the application of gentle heat.

If the urine contain mucin in excess, a light cloud may come into view *toward the surface* of the urine with this test. It will be remembered that mucin is soluble in strong nitric acid, but is precipitated by the same in dilute form, and therefore the mucin reaction always occurs high up in the strata of urine which contains the acid well diluted. If the urine contain the pine acids a reaction may occur with this test somewhat similar to that of albumin, though usually less defined. The precipitate due to oleo-resins is soluble in alcohol, which distinguishes it from that due to albumin.

The nitric-acid test precipitates all modifications of albumin, acid and alkaline, as well as albumose. On the other hand, it gives no reaction with peptone or the vegetable alkaloids.

4. *The Ferrocyanic Test.*—This test is exceedingly simple and rapid in application, as follows: Into the bottom of a clean test-tube is poured 15 to 30 drops of acetic acid, then about two or three times that amount of solution of potassium ferrocyanide (1 to 20) is added, and the two thoroughly mingled by shaking the tube. The urine is next added, to the depth of two-thirds of the test-tube. If albumin be present it will be precipitated throughout the whole volume of the urine in the form of a more or less milk-like, flocculent cloud, according to the quantity of albumin present. The ferrocyanic test *applied by the above method* avoids the mucin reaction, and precipitates all modifications of albumin, acid and alkaline. On the other hand, it gives no reaction with phosphates, urates, peptones, the vegetable alkaloids, or the pine acids. This test may also be applied as follows: Fill an ordinary test-tube half full of urine, and add a drachm or so of potassium-ferrocyanide solution (1 in 20). After thorough mingling of the urine and reagent, add a few drops (10 to 15) of acetic acid, and if albumin be present it will come plainly into view. This is a most trustworthy test, if applied by either of the above methods, and it may be depended upon for the detection of albumin in the urine, either in large or small amounts, without further corrections or precautions. Any precipitate produced by this test, when applied as above, *is albumin, and nothing but albumin.*[1]

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[1] It is improper to apply this test by previous acidification of the urine, because it is only by adding the ferrocyanide solution to the urine first or with the acid that the latter is prevented from precipitating the urinary mucin.

OTHER TESTS FOR ALBUMIN.

The last few years have greatly contributed to the number of tests for albumin in the urine; the more prominent of those brought forward are the following:—

5. *Potassio-Mercuric Iodide Test.*—This solution was first proposed by Tanret as a most sensitive test for albumin. The formula is as follows: Potassium iodide, 3.32 grammes; bichloride of mercury, 1.35 grammes; acetic acid, 20 cubic centimetres; distilled water to 100 cubic centimetres. The potassium iodide and mercuric chloride should be separately dissolved in water, and the solutions mixed; the resulting reagent is the double iodide of mercury and potassium, to which the acetic acid is added, and the whole made up to 100 cubic centimetres with distilled water. As thus prepared the test is applied by the contact method; the reagent, being of specific gravity of about 1040, is introduced into the test-tube first, and the urine allowed to overlay it in the usual manner.

The test may also be applied by keeping the acid and the mercuric-iodide solution separate. The urine is then acidified, first with acetic acid, and the reagent added to half a test-tubeful of urine, and if albumin be present it is immediately caused to fall out of solution in a white cloud, more or less pronounced, according to the quantity present.

The test responds to all modifications of albumin, also to peptone and the proteoses, as well as the vegetable alkaloids and pine acids. All reactions, however, other than with albumin, the pine acids, and mucin, disappear upon gently heating. This test is one of great sensitiveness in bringing to light minimal traces of albumin.

6. *Picric Acid.*—This test has been strongly advocated by Sir George Johnson, of London. The test is made by saturation,—6 or 7 grains to the ounce of boiling distilled water. Upon a column of urine four inches deep in an ordinary test-tube is gently floated the reagent, and in consequence of its low specific gravity it only mixes with the upper layer of urine. As far as the yellow color of the picric-acid solution extends, the coagulated albumin renders the mixture turbid, forming a contrast with the clear urine below. There must be an actual mixture, not mere contact of the urine with picric acid. This test precipitates albumin, peptone, mucin, proteoses, as well as the vegetable alkaloids, all of which, save mucin, are dissolved by heat.

7. *Sodium Tungstate.*—This test was suggested by Dr. George Oliver as a most sensitive reagent for albumin. The solution is made by mixing equal parts of sodium-tungstate solution (1 to 4) and saturated solution of citric acid (10 to 6). Dr. Oliver applies the test by the contact method. This test precipitates, in addition to albumin, peptone, mucin, and occasionally the urates. It gives no reaction, however, with the alkaloids, and all precipitates, save those due to albumin and mucin, are dissolved by gentle heat.

8. *Acidulated Brine Test.*—This test was suggested by Roberts, and is prepared by mixing together a pint of saturated solution of sodium chloride and 1 fluidounce of strong hydrochloric acid, and filtering. The test is applied by the usual contact method, the reagent being introduced into the test-tube first, and the urine gently floated thereupon.

9. *Nitric Magnesium Test.*—This test, also suggested by Roberts, is composed

of 1 ounce of strong nitric acid and 5 ounces of saturated solution of magnesium sulphate. This is claimed to be more sensitive than the nitric-acid test, and is applied by the contact method.

10. *Phenic-Acetic-Acid Test.*—This test was brought forward by Millard as the most sensitive of all albumin reagents. The formula is as follows: Acid phenic glacial (95 per cent.), ʒij; acid acetic (C.P.), ʒvij; liquor potassæ, ʒvj. This test is applied in the usual contact manner by overlaying the reagent with the suspected urine. In addition to precipitating albumin, this reagent throws down peptone, mucin, alkaloids, and the pine acids,—the peptone and alkaloids being dissolved upon the application of heat.

11. *Trichloracetic-Acid Test.*—This solution is prepared by simply saturating distilled water with the crystals of trichloracetic acid (about ℥ss to ℥j of water). The test is applied by the contact method, and delicate results are claimed for this reagent.

12. *Heynsius's Test.*—The urine is rendered strongly acid with acetic acid; a few cubic centimetres of saturated solution of sodium chloride are added, and the mixture boiled. The presence of albumin is shown by the appearance of a flocculent precipitate.

13. *Heidenlang's Test.*—This test simply consists in adding to the suspected urine a little solid metaphosphoric acid, and, if albumin be present, coagulation occurs in the form of a white precipitate.

14. *Acetic Acid and Sodium Sulphate.*—Acidulate the urine strongly with acetic acid; add 1 drachm of the strongly acid urine to 1 drachm of a strong solution of sodium sulphate and boil. If albumin be present a permanent precipitate will result.

15. *Biuret Test.*—The urine is treated with caustic potassium, and a dilute solution of cupric sulphate is added, drop by drop, by means of a pipette. If albumin be present, the resulting cupric peroxide (a green precipitate) is dissolved, and the fluid assumes a reddish-violet color. This test reacts with albumin, albumose, globulin, and peptone,—the latter substance, however, giving a red, not violet, color.

16. *Millon's Reaction.*—Add to 1 drachm of the urine 10 minims of Millon's reagent, and heat. If albumin be present in considerable quantities, a white precipitate will appear, which will become red when heated. If only a trace of albumin be present, no precipitate is formed, but the fluid becomes red. This reaction is common to all the monohydroxol-benzol derivations, and is ambiguous, since the reaction can be obtained from bodies of the aromatic series.

17. *Xanthoproteic Reaction.*—Add to the sample of urine concentrated nitric acid and boil. Let the liquid cool, and then add ammonium. If albumin be present an orange color is produced.

About ten years ago the author made some study of the then newer tests for albumin[1] in the urine, especially including Nos. 5, 6, and 7. Very recently he has subjected practically the whole series to a most crucial examination, with a view of determining their practical value for clinical purposes. The conclusions reached are as follow: While many of these later tests—notably 5, 6, 7, 8, 9, 10, and 11—are exceedingly delicate reagents for albumin, greatly exceeding in sensitiveness the older methods,—as, for instance, with heat and nitric acid,—yet their increased sensitiveness is nearly always obtained at the expense of trustworthiness. Without exception, the tests named give a reaction with substances in normal urine, or with substances in abnormal urine other than albumin. Furthermore, some of these reactions cannot be distinguished from the albuminous reaction without further testing, and even in some cases without an appeal to some other test. Sir William Roberts claims that the most common source of fallacy is with mucin. While the author believes that mucin is not the exclusive source of error, especially with those reagents for which unusual sensitiveness is claimed,—nucleo-albumin, as well as proteids of no grave pathological significance, being often responsible for these reactions,—yet he believes that the mucin reaction is positively avoided in but two tests in the whole series,—viz., in Nos. 2 and 4. If a pure solution of mucin be prepared and normal albumin-free urine be heavily charged with this solution, the following reactions may be observed: (*a*) Upon the addition of a few drops of nitric acid to such a urine in a test-tube a distinct, albumin-like precipitation at once appears, which boiling, however long, fails to remove. If the process be reversed and heat be first applied, and subsequently the acid be added, the result is precisely the same. (*b*) If now we follow the principle of test No. 2, and first raise the specific gravity of the urine by a saline such as sodium chloride to 1035, and then add *one* or *two* drops of acetic acid and boil, no precipitate whatever appears, because, while acetic acid is a sensitive precipitant of mucin, yet in solutions rich in salines mucin will not be precipitated by acetic acid even in very considerable quantity. (*c*) If next the muciparous urine be submitted to test No. 3,—Heller's nitric-acid method,—a very distinct reaction results. (*d*) If the urine be subjected to No. 4, we find that the ferrocyanic solution acts as does the saline (sodium chloride) and prevents the precipitation of the mucin by the acetic acid, and no precipitate results. (*e*) If next the muciparous urine be subjected to tests 5, 6, 7, 8, 9, 10, 11, 12, 13, and 14, a very distinct reaction will become visible in most, if not in all, cases, but more especially marked, perhaps, in 5, 6, 7, 8, 10, 11, and 13. As a rule, the more highly acid the urine (normal acidity), the more sharp will be the reaction, and this corresponds with the oft-mentioned fact that these highly-sensitive tests give reactions with most urines of high specific gravity. It is evident from the above observations that our methods of testing for albumin in the urine, even with some of the older routine tests, need revision.[1]

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[1] "The Comparative Value of the Newer Tests for Albumin in the Urine," Journal of the American Medical Association, January 19, 1884.

While, doubtless, it is desirable that we should possess tests for albumin of somewhat greater sensitiveness than the old and somewhat crude method of boiling the urine, yet, after all, extreme delicacy of reaction is altogether a matter of secondary consideration, as compared with accuracy, because, when the quantity of albumin in the urine is *very slight*, resort must necessarily be had to other means than the presence of *traces of albumin* in the urine, in order to be able to establish a positive diagnosis of renal disease. Notwithstanding the above facts, much unnecessary confusion and uncertainty in our present methods have been caused by the multiplication of tests for albumin in the urine whose chief claim for recognition is that of great sensitiveness of reaction rather than that of trustworthiness. On the other hand, it is not the newer methods that are alone responsible for all the errors that are encountered in searching for albumin in the urine. Indeed, the very oldest method in use,—that with heat and nitric acid,—unfortunately, requires precautions and corrections so perplexing, in order to be absolutely reliable, that authors themselves are by no means agreed as to the safest method of its application.

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[1] Many of the newer tests for albumin call for the previous acidification of the urine by some acid. This necessarily precipitates the mucin of the urine, if present in excess, and the addition of the reagent usually intensifies this mucin reaction. Now, it is well known that in all highly-concentrated urines there is present a more or less excess of mucin, and it seems irresistible to conclude that in this class of tests the faint reaction noted so commonly in urines of high specific gravity is very often due to mucin rather than to minimal traces of albumin. Any acid will thus act with mucin unless special precautions be taken to prevent it. The strong mineral acids, by the contact method, become diluted by the strata of urine *near the plane of contact*, and this dilution permits precipitation of the mucin, if present in excess. The vegetable acids need no dilution, but throw out mucin at once, either when mixed with the urine or upon contact, in the latter case *at the point of contact*. For these reasons the author has, from long experience, come to be somewhat suspicious of tests for albumin which require previous acidification of the urine, when searching for *minute traces of albumin*. If we wish to avoid the mucin reaction, it can only be done in the presence of albumin precipitants, by first charging the urine with some salt that prevents precipitation of the mucin; and while the albumin precipitant may thus act if mingled with the urine, by previous acidification of the urine it usually only intensifies the mucin reaction.

18. *Tests in Paper Form.*—According to the suggestion of Dr. George Oliver, of Harrogate,[1] a number of the tests named have been prepared and used in paper form. This is accomplished by saturating chemically inert filtering-paper with solutions of the albumin reagents, and with citric acid and then drying. The papers are then cut into slips of convenient size for testing, and may be carried about in the pocket-case for use at the bedside of the patient. In testing, the following method is followed: Into a small test-tube containing one drachm of distilled water are dropped a reagent paper and one charged with citric acid. After agitation for a minute or so the test-papers are removed and the solution is ready for testing. The urine is now added, and the test may be conducted either by a mixture of the two or by the contact method, of which Dr. Oliver advises the latter.

Dr. Oliver now advises the use of two reagents only for albumin, viz., the ferrocyanic and potassio-mercuric papers. The former of these will be found trustworthy, and of very great convenience in clinical work in the hospital wards or at the bedside, if applied in accordance with the principles laid down by the author in using the ferrocyanide test, *i.e.*, by using the reagent first and the acid last.

Method of Testing for Albumin in the Urine.—If the quantity of albumin in the urine be large, the use of any of the first four tests described will unmistakably reveal its presence. It is only in searching for the smaller quantities of albumin that errors are likely to be encountered in testing ; since a number of substances are often present in the urine which may give precipitates strongly resembling those due to albumin in small amounts.

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[1] Bedside Urine Testing. London, 1885.

In searching for albumin in the urine a test should be selected for routine work which is trustworthy, ready of application, requiring the fewest possible precautions, and possessing reasonable delicacy of reaction. In these respects, No. 4,—the ferrocyanic test,—is the most desirable in the list described. This test is recommended for routine work because it requires the fewest precautions, while in point of delicacy it is at least equal to nitric acid or heat, in whatever form applied. This test gives no reaction with peptone, mucin, the vegetable alkaloids, urates, or the pine acids, while it sharply reacts with all modifications of albumin, whether acid or alkaline.[1]

It has been stated that the ferrocyanic test occasionally precipitates the urates of the urine as a source of error. The author has used the test daily for over ten years without meeting such reaction. Those who still prefer to work with the old method of heat and acid will do well, *when dealing with minute quantities of albumin*, to follow the course advised in No. 2, thereby avoiding the possible mucin reaction.

Test No. 3, Heller's nitric-acid method, is one of considerable delicacy. It will, however, precipitate mucin, which slowly settles down to the point of contact between the two fluids; and when it is remembered that in the presence of minute quantities of albumin it requires twenty or thirty minutes to bring out the latter, it will be seen that there is no certain method of distinguishing between the two. The same may be said with reference to its behavior with urates, save that the latter may be made to disappear by heat.

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[1] Over ten years since, the author claimed (Journal of the American Medical Association, January 19, 1884) that the ferrocyanic test for albumin was the most ready and trustworthy of the list. Again, in 1886, the author wrote (Bright's Disease and Allied Affections of the Kidneys, p. 43) : "Subsequent use has shown me that this test is the least liable to errors of all tests for albumin in the urine, if properly applied." The fact that within the past five years the ferrocyanic test has been given the preference in many of the leading laboratories and clinics in Continental Europe over all others only confirms the author's views both then and now.

Finally, in searching for albumin in the urine, it is sometimes useful to have a test of extreme delicacy of reaction purely for negative purposes. As such, the potassio-mercuric iodide solution is probably the most desirable. If, for instance, no reaction be obtained by this reagent, it is certain that no albumin whatever is present in the urine; and, furthermore, the urine is absolutely free from all known proteids. The author strongly advises the future disuse of all albumin tests, from No. 5 to No. 14 inclusive, for clinical purposes,—save for negative or differential information,—for his experience has shown him that they are undoubtedly misleading and untrustworthy.

Determination of Albumin in the Urine.—The quantity of albumin in the urine is most accurately determined by the "Gravimetric Method," as follows: 100 cubic centimetres of the urine are treated with a mixture of equal parts of ferrocyanic solution (saturated) and acetic acid, which is added drop by drop until all the albumin is precipitated, after which the fluid is passed through a filter of known weight. The precipitate on the filter is next washed successively with water, alcohol, and ether, and dried at a temperature of 120° C. The filter, with its contained albumin, is next weighed, and the difference in weight due to the precipitate is the weight of the albumin in 100 cubic centimetres of urine.

The above process is altogether too tedious for clinical purposes, and moreover it is, strictly speaking, unnecessary. It serves no practical purpose to know the exact number of grains of albumin in a given specimen of urine, because the severity of the disease cannot be accurately gauged by such knowledge. On the other hand, it is of great practical utility to be able to estimate the *relative quantity* of albumin in the urine from day to day, in order to be able to determine the progress of the disease and the results of treatment.

It is much to be regretted that we possess no standard method of expressing the quantity of albumin in the urine, in consequence of which, as Dr. Tyson correctly observes, "There is much carelessness of expression among physicians in speaking of the quantity of albumin found in a given specimen of urine." Thus, bulk measure by precipitation is often spoken of as percentage amount, and hence we often hear of urines containing 50 and even 75 per cent. of albumin, when, as a matter of fact, the urine never contains to exceed 3 or 4 per cent. by actual weight. The expression, *percentage*, therefore, should be qualified by the statement of the measurement, whether it be by bulk or weight.

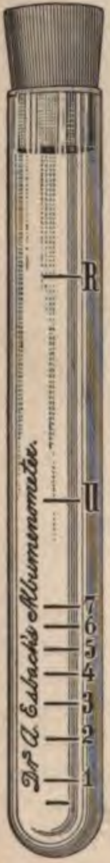

FIG. 8.—ESBACH'S ALBUMINOMETER.

Esbach's Method.—This test is made by means of a standard graduated glass tube or albuminometer, as shown in the figure. The process is as follows: The following standard solution is prepared: Picric acid, 10 grammes; citric acid, 20 grammes; distilled water, to 1000 cubic centimetres (1 litre). Fill the albuminometer tube with the urine to the letter *U*, then add the test solution to *R*, close the tube with the stopper and invert several times, until the urine and the test solution are thoroughly mixed. Stand the tube in a rack for twenty-four hours and then read off the number of grammes of albumin to the litre, as will be indicated by the number on the side of the tube on a level where the albumin settles. If it be desired to know the percentage of albumin in the urine instead of the number of grammes per litre, remove the decimal point one figure to the left; thus 5 grammes per litre would be 0.5 per cent. of albumin. It will be observed that Esbach's albuminometer tubes are so graduated that their highest range is 7 grammes per litre, 0.7 per cent. of albumin. If, therefore, the urine be highly albuminous, it should be diluted with one or two volumes of water before testing, and the product multiplied by two or three, according as the volume is doubled or trebled. These albuminometer tubes are supplied by Eimer & Amend, of Third Avenue, New York, at moderate cost.

In order to get immediate results the author places these albuminometer tubes in the centrifugal machine, when the albumin is precipitated in three or four minutes. It is found that, as soon as the albumin settles so that the fluid above is clear by centrifugation, the instrument reads practically the same as standing for twenty-four hours. Centrifugation is also found to possess the following advantages: It obviates the occasional failure of the albumin to settle in the bottom of the tube; the specific gravity of the urine does not materially influence the uniform settling of the albuminous sediment.

The Author's Centrifugal Method.—With the author's electric centrifuge this method can be carried out very rapidly (within five minutes), and the results are all that are desirable for practical purposes. Process: The percentage tubes (see p. 64) are filled to the 10-cubic-centimetre mark with the urine to be tested, and 3½ cubic centimetres of potassium-ferrocyanide solution (1 in 10) are added; 1½ cubic centimetres of acetic acid are next added, and the reagents and urine are thoroughly mingled by closing and several times inverting the tubes. The tubes are next placed in the centrifuge and revolved until all the albumin has settled, leaving the fluid above perfectly clear. The bulk percentage of albumin is then read off, each $\frac{1}{10}$ cubic centimetre representing 1 per cent. bulk measure of albumin.

Esbach's method is supposed to measure the amount of dry albumin by weight, but, unfortunately, Esbach's reagent (picric acid) throws out and measures peptones, mucin, the proteoses, and practically all the proteids of the urine, and, therefore, the author finds that it is subject to almost constant and wide errors.

The author's centrifugal method, on the other hand, throws out and measures *all the albumin*, and practically nothing else. In carrying out the centrifugal method it will be found necessary, if the urine be very highly albuminous, to dilute with one or two volumes of water, and multiply the result, accordingly, by two or three.

In taking the measurement of albumin by the centrifugal method the following rule should be observed, to insure uniform results: *Leave the percentage tubes in the centrifuge until all the albumin is fully precipitated and the urine above is perfectly clear, then read the amount.* This method quickly and definitely determines the amounts of albumin in the urine from day to day, and more minutely measures the degree of increase or diminution than is possible with Esbach's method, because the unit of Esbach's albuminometer is 1 gramme, which, if measured by the author's percentage tubes, would correspond to nearly 18 per cent. (or 18 units).

PROTEOSES.

These substances are the intermediate products in the hydration of proteids, the final products being peptones. In the body they are formed by the action of the gastric and pancreatic juices, and they may be formed artificially by heating albumin with water,—more readily by dilute mineral acids or sulphuretted steam. They correspond to the propeptone of Schmidt-Mulheim, and to the A-peptone of Meissner. They are uncoagulable by heat, are precipitated but not coagulated by alcohol; they all respond to the biuret reaction, and are precipitated by nitric acid, the precipitate thus formed being dissolved by heat, but re-appearing upon cooling.

These substances may be subdivided into albumoses, globuloses, vitelloses, caseoses, myosenoses, depending upon the proteid from which they are formed. The albumoses and globuloses are absent from normal urine, but appear in the urine under a number of abnormal conditions.

Albumosuria.—The albumoses are of two varieties: *hemi-albumoses*, or those convertible by further digestive action into *hemi-peptone*, and *anti-albumoses*, or those similarly converted into *anti-peptone*. Albumoses have also been classed according to their solubilities, as follows: (*a*) Proto-albumose; soluble in cold and hot water, and in saline solutions. They are precipitated as are globulins, by saturation with sodium chloride and magnesium sulphate. (*b*) Hetero-albumose; insoluble in water; soluble in 0.5 to 15 per cent. sodium-chloride solutions in the cold, but precipitable by heat at 65° C., the precipitate being readily soluble in dilute acid or alkali. It is precipitated by alcohol as is other albumoses, but, unlike them, it is partly converted into an insoluble *dys-albumose*. Hetero-albumose is precipitated by dialyzing out the salines from its solutions, and, like proto-albumose, it is precipitated by saturation with salines. Proto- and hetero- albumoses constitute the first products of the hydration of proteids, and have hence been called primary albumoses. (*c*) Deutero-albumose is soluble in cold and hot water, is not precipitated from its solutions by saturation with sodium chloride or magnesium sulphate, but it is precipitated by strong solutions of ammonium sulphate. It is not precipitated by copper sulphate, and only gives the nitric-acid reaction (characteristic of albumoses) in the presence of excess of saline. It is therefore, in reactions, nearest to peptones of the albumoses; it is an intermediate stage in the conversion of primary albumoses into peptone.

Clinical Significance.—Albumose, like peptone, is found in pus; but, unlike the latter, it is also present in the blood, most notably so during digestion. An albumose was first discovered in the urine by Bence Jones in a case of osteomalacia, and in a like case since by Kuhn. Virchow has found this albumose in the medulla of bones in osteomalacia, while Fleischer found it in the medulla of normal bone. Senator has found albumoses in a number of cases in the urine,—viz., tertiary syphilis, hemiplegia, double pneumonia, diphtheria, carcinoma, and muscular atrophy. Hoppe-Seyler has found it in a number of cases of atrophy of the kidneys. Lassar has found it in the urine of people rubbed with petroleum, while Oertel has met with it in a few cases after severe exertion. Albumose and peptone are both found in the urine of animals when injected into their circulation. Deutero-albumose so closely resembles peptone in its reactions that it is often mistaken for the latter substance. Its distinction from peptone will be considered in connection with peptonuria. The clinical significance of albumosuria, so far as our present knowledge extends, is very indefinite; so that practical conclusions in connection with its presence in the urine are as yet lacking. In the few diseases in which it has been noted, its appearance, under similar circumstances, has subsequently been found inconstant.

Detection.—The proteoses are known by their solubilities and reactions, as follows: *Proteo-albumose*, soluble in both hot and cold water, in both hot and cold saline solution (10 per cent.

NaCl), is precipitated with strong solutions of sodium chloride and magnesium sulphate; also by saturated solution of Am_2SO_4; is precipitated by nitric acid in the cold; not soluble on heating, or only slightly so; it is precipitated by copper sulphate.

Hetero-albumose, insoluble in hot and cold water, is precipitated by dialysis from saline solutions; soluble in both hot and cold solutions of sodium chloride of 10-per-cent. strength,—*i.e.*, is partly precipitated, but not coagulated, on heating to 65° C.; is precipitated by saturation with sodium chloride or magnesium sulphate; also with saturated ammonium sulphate; and is precipitated by nitric acid in the cold, the precipitate being dissolved with heat and re-appearing on cooling.

Deutero-albumose is soluble in hot and cold water; soluble in hot and cold solutions of sodium chloride of 10-per-cent. strength; *is not precipitated* by saturation with sodium chloride or magnesium sulphate, but is precipitated by saturation with ammonium sulphate; while with nitric acid it is only precipitated in the presence of excess of salt.

PEPTONURIA.

Peptones are best known as the final products of gastric and pancreatic digestion. They are also products of retrogressive changes in albuminoids and of the corpuscular elements of the blood, and as such assume importance in their clinical relations. It has just been stated that peptones are the final products of gastric and pancreatic digestion. If hydration were continued a step farther, peptone would be split up into simpler substances, and would no longer constitute a proteid. Peptones are soluble in water, uncoagulable by heat, and are not precipitated by nitric acid, copper sulphate, ammonium sulphate, potassium ferrocyanide, and a number of other precipitants of proteids. They are precipitated by tannin, potassio-mercuric iodide, phosphomolybdic acid, phosphotungstic acid, and picric acid.

Peptones are divisible into two forms: (*a*) *Hemipeptone*, which by further action of the pancreatic juice is split up into leucin and tyrosin and such simpler products. (*b*) *Antipeptone*, which is not decomposed further by pancreatic juice. It, furthermore, does not yield tyrosin on treatment with sulphuric acid, and does not respond to Millon's reagent.

Both forms of peptone are readily diffusible through animal membranes, albumoses being only slightly so, and albumin not so at all, under ordinary circumstances. The peptones are not precipitated by saturation with ammonium sulphate, in which respect they differ from albumoses.

Clinical Significance.—Peptone is absent from normal urine, but has been described in the urine in connection with numerous pathological conditions. Since the recent publication of Kuhn and Chittenden's work on proteoses and peptones, it has been made evident that many of the cases formerly described as peptonuria were, in reality, albumosuria, the real proteid present being deutero-proteose, and, therefore, much of our supposed knowledge of peptonuria needs revision.

Peptonuria has been frequently described as associated with the following conditions: In phosphorus poisoning, in suppurative diseases, in croupous pneumonia, acute rheumatism, typhoid fever, typhus, small-pox, scarlet fever, mumps, tuberculosis, erysipelas, empyema, cancer of the viscera (notably of the liver and intestines), catarrhal jaundice, apoplexy, etc. The local—sometimes termed the pyogenic—causes seem to be connected with resorption of exudations so situated as to favor the products of disorganization—the peptone constituent of leucocytes—being absorbed into the circulation, from whence it is eliminated by the kidneys. This form of peptonuria is met with in the declining stages of pneumonia, in purulent pleuritis, suppurating tuberculosis, chronic bronchial catarrh, psoas abscess, purulent meningitis, and acute articular rheumatism.

In acute inflammatory affections the appearance of peptonuria may be taken as an evidence that suppurative changes have been established, other known causes of peptonuria being excluded. Jaksch insists that, as a means of distinguishing between tubercular and epidemic cerebro-spinal meningitis, peptonuria is of crucial significance, being absent in the former and characteristic of the latter. In this connection, however, ulcerative changes in the lungs must be excluded to render this sign trustworthy.

In like manner, peptonuria appearing as is usual in septicæmia may serve to distinguish it from latent disseminated sarcoma when, as often happens, the clinical symptoms are very similar. In short, Maixner has declared it the law that peptone is always present in the urine when pus is forming in the organism.

In addition to the pyogenic causes of peptonuria, extensive destruction of the corpuscular elements of the blood seems to constitute a prominent cause, and hence the frequent appearance of peptonuria in acute infectious diseases and toxic conditions already enumerated.

Peptonuria also arises from a few additional causes. It is almost invariably associated with cancer of the liver, and this fact has led Pecancowski to the conclusion that the liver in health is concerned in the conversion of peptone into albumin. Maixner has shown that in ulceration of the intestines the peptic products of the stomach pass directly into the blood through the ulcerated surfaces, and give rise to peptonuria. Then, again, we have puerperal peptonuria, Fischel having shown that peptone is a normal constituent of the urine in the puerperal condition. Finally, when injected into the blood, peptone quickly appears in the urine.

Detection.—Peptone may be recognized by the following method: Saturate the urine (slightly acidified first with acetic acid) with ammonium sulphate, and filter out any precipitate formed which may consist of albumin, globulin, proto-albumose, hetero-albumose, or deutero-albumose. Any proteid remaining may be precipitated by potassio-mercuric iodide or picric acid, and can only be peptone. This is, in fact, the only certain method of identification of peptone.

Differentiation.—Since peptone and deutero-albumose so closely resemble each other in reactions, it is well to be able to distinguish them, more particularly since the frequency with which they have been confounded has undoubtedly led to numerous clinical errors. Halliburton contrasts them as follows:—

PEPTONE.	DEUTERO-ALBUMOSE.
1. Gives no precipitate with nitric acid.	1. Gives no precipitate with nitric acid unless a considerable amount of salt be added. This precipitate disappears on heating and re-appears on cooling.
2. Is not precipitated by saturation with ammonium sulphate.	2. Is precipitated by saturation with ammonium sulphate.

In all other respects these two substances, as far as known, behave similarly.

Recent researches by Kuhn[1] have shown that, in order to effect complete separation of the albumoses from peptones, the mixture containing these substances should be saturated *whilst boiling* with ammonium sulphate. Furthermore, a single saturation with ammonium sulphate should not be depended upon to remove all the deutero-albumose, but saturation should be repeated till precipitation no longer occurs.

GLOBULINURIA.

Globulin is insoluble in water, but dissolves in dilute neutral salt solutions. From these solutions it is precipitated by sufficient dilution with water, and on heating it coagulates. Globulin dissolves in water on the addition of very little acid or alkali, and on neutralizing the solvent it re-precipitates. Solutions of globulin in a minimum amount of alkali are precipitated by carbon dioxide, but the precipitate may be dissolved by excess of the precipitant. The neutral solutions of globulin containing salts are precipitated on saturation with sodium chloride and magnesium sulphate at normal temperatures. Normal urine is free from globulin, but this proteid appears in the urine in a number of pathological conditions.

Clinical Significance.—Globulinuria is nearly always associated with albuminuria, and, indeed, globulin may greatly exceed the quantity of albumin present in some cases, although the proportion of globulin in the blood is only as 1 to albumin 1.5. Globulin is, however, a more diffusible form of proteid than albumin, which may account for its proportional excess in the urine at times. From the fact already stated, that globulin is nearly always associated with albumin in the urine, its clinical significance is nearly identical with that of albuminuria. In a few cases, however, its presence in the urine seems to imply a special significance. Thus, globulin is noted in unusual quantities in the urine in catarrhal inflammations of the bladder, in acute nephritis, and especially in amyloid degeneration of the kidneys. The same is said to be the case in albuminuria associated with digestive disorders. On the other hand, in chronic Bright's disease globulin is said to be present in very small amount, or even at times absent.

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[1] W. Kuhn, Erfahrungen über Albumosen und Peptone, I. Reinigung der Peptone von Albumosen. Separatabdruck aus der Zeitschrift f. Biologie, 1893.

Detection.—1. Exactly neutralize the urine, filter, and treat with magnesium sulphate in substance until it be completely saturated at an ordinary temperature, or with a saturated solution of ammonium sulphate. In both cases a white precipitate is formed if globulin be present. In using ammonium sulphate with urines rich in urates, precipitation of ammonium urate may appear. These, however, do not immediately appear, but only after some time, and they may thus be distinguished from the globulin precipitate.

In detecting serum-albumin in the same urine, heat the filtrate after precipitation of the globulin to boiling, after the addition of a few drops of acetic acid.

2. Globulin falls out of solution when the urine is diluted until the specific gravity is about 1002, and upon the above fact Roberts suggested the following simple test: Fill a wineglass or test-tube with water and let fall into it several drops of albuminous urine. If globulin be present in any quantity, each drop as it falls is followed by a milky streak, and when a number of drops have been added the water assumes a milky opalescence throughout. The addition of acetic acid causes the opalescence to disappear.

Determination.—The separate determination of globulin and albumin may be accomplished by carefully neutralizing the urine and precipitating with magnesium sulphate added to saturation, or by simply adding an equal volume of saturated solution (neutral) of ammonium sulphate. The precipitated globulin is thoroughly washed with saturated magnesium sulphate, or half saturated ammonium-sulphate solution, dried at 110° C., boiled with water, extracted with alcohol and ether; then dried, weighed, and ashed; then weighed again, and the weight is the amount of globulin.

DIFFERENTIAL TESTING.

Serum-albumin, serum-globulin, hetero-proteose, deutero-proteose, and peptone may all be present in the urine simultaneously. This is very unusual, but in doubtful cases the only certain method is to test for each one in the list. The best method of doing this is that proposed by Halliburton, as follows:—

1. If the urine give no precipitate on boiling after acidulation, albumin and globulin are absent. If a precipitate occur, albumin or globulin, or both, are present.

2. If the urine after neutralization give no precipitate on saturation with magnesium sulphate, globulin and hetero-proteose are absent. If such precipitate occur, one or the other is present.

3. If the urine be saturated with ammonium sulphate and filtered, and the filtrate gives no xanthoproteic or biuret reaction (a large excess of potash must always be added), peptone is absent.

4. If the urine give no precipitate on boiling after acidulation, no precipitate with nitric acid, and no precipitate on adding ammonium sulphate to saturation, peptone can be the only proteid present. Confirm this by the biuret reaction.

5. If all proteids are present, they may be separated as follows:—

Saturate the urine (faintly acidified with acetic acid) with ammonium sulphate. A precipitate is produced. Filter.

(*a*) PRECIPITATE.	(*b*) FILTRATE.
Contains albumin, globulin, hetero- and deutero- proteose.	Contains peptone.

Collect the precipitate on a filter, wash it with saturated solution of ammonium sulphate, and redissolve it by adding a small quantity of water. To this solution add ten times its volume of alcohol; a precipitate is formed; collect this, and let it stand in absolute alcohol for from seven to fourteen days. Then filter off the alcohol, dry the precipitate at 40° C., extract with water and filter. An insoluble residue is left.

(*a*) RESIDUE.	(*b*) EXTRACT.
This consists of albumin and globulin coagulated by alcohol.	This contains the proteoses in solution.

Hetero-proteose is precipitated by heating the solution to 65° C., or by saturating a portion of the extract with magnesium sulphate. Deutero-proteose remains in solution.

Take another portion of the urine, neutralize it, and saturate with magnesium sulphate. A precipitate is produced. Filter.

(*a*) PRECIPITATE.	(*b*) FILTRATE.
This consists of globulin and hetero-proteose, which may be separated by the prolonged use of alcohol, as above.	This contains albumin, deutero-proteose, and peptone. Add alcohol, as above; albumin is rendered, in seven days, insoluble in water. The deutero-proteose and peptone are soluble, and may then be separated by ammonium sulphate.

The reactions of the several proteids in the urine already considered may be seen at a glance in the following table, after Halliburton. (See next page.)

HÆMOGLOBINURIA.

Hæmoglobin, the red pigment of the blood, is a somewhat remarkable compound in that it contains iron, is intimately associated with a proteid, and gives the proteid reaction; it is hence non-diffusible, but yet is crystalline. It exists in the blood in two conditions,—in arterial blood it is termed oxyhæmoglobin, being charged with oxygen; in venous blood it is deoxygenated or reduced hæmoglobin. Hæmoglobin belongs to the group of blood-proteids, which yields splitting products and small amounts of volatile fatty acids with about 96 per cent. albumin and about 4 per cent. hæmochromogen, containing iron, which, in the presence of oxygen, is readily oxidized into hæmatin. Hæmoglobin prepared from different kinds of blood has not always the same constitution, indicating the probable presence of different hæmoglobins. This is further shown by the facts that different kinds of blood also differ in solubility and crystalline form, and possess a varying quantity of water of crystallization.

The Clinical Significance.—The blood-pigment, hæmoglobin, sometimes appears in the urine without the appearance of any

TABLE OF REACTIONS OF PROTEIDS IN THE URINE.

Variety of Proteid.	*Hot and cold water.*	*Hot and cold saline solution, e.g., 10 per cent. $NaCl$.*	*Saturation with $NaCl$ or $MgSO_4$.*	*Saturation with Am_2SO_4.*	*Nitric acid.*	*Copper sulphate.*	*Copper sulphate and ammonia.*	*Copper sulphate and caustic soda, or potash.*
Albumins.	Soluble in cold and coagulated in hot water.	Soluble in cold and coagulated in hot solutions.	Not precipitated.	Precipitated.	Precipitated in cold; not dissolved by heating.	Precipitated.	Blue solution.	Violet solution.
Globulin.	Not soluble in either.	The same as albumins.	Precipitated.	Precipitated.	The same as albumins.			
Proteo-albumose.	Soluble in both.	Soluble in both.	Precipitated.	Precipitated.	Precipitated in cold; precipitate dissolves with heat and returns in cold.	Precipitated.	Violet solution.	Rose-red solution.
Hetero-albumose.	Insoluble, *i.e.*, like globulins, precipitated by dialysis from saline solutions.	Soluble in both; partly precipitated but not coagulated by heat to 65° C.	Precipitated.	Precipitated.	"	"	"	"
Deutero-albumose.	Soluble.	Soluble.	Not precipitated.	Precipitated.	Only reacts in presence of excess of salt.	Not precipitated.	"	"
Peptone.	Soluble.	Soluble.	Not precipitated.	Not precipitated.	Not precipitated.	Not precipitated.	"	"

corpuscles associated therewith, as was first shown by Pavy. This is always the result of the destruction of the blood-corpuscles in the circulating stream. The hæmoglobin thus liberated is thrown out by the kidneys and appears in the urine. This may be produced by injection into the circulation of substances which act as solvents of the corpuscles, such as glycerin, solutions of the bile-salts, distilled water, and the injection of the blood of one animal into another. Similar results follow in cases of poisoning with arseniuretted hydrogen; hydrochloric, sulphuric, carbolic, and pyrogallic acids; phosphorus, and potassium chlorate. In certain diseases, notably pyæmia, typhus, scurvy, fat-embolism, in some cases of jaundice, and after extensive burns, hæmoglobinuria often results. The most interesting and marked pathological condition in which hæmoglobin appears in the urine is the disease known as *paroxysmal hæmoglobinuria*, which will form the subject of special consideration in a subsequent section of this work.

Detection.—1. Solutions of hæmoglobin may be determined by spectroscopic examination with great precision. They strongly absorb the rays lying between *C* and *D*. In a proper dilution the solution shows a spectrum with one broad, not sharply-defined band between *D* and *F*. This band does not lie in the middle, between *D* and *E*, but is toward the red end of the spectrum, a little over the line *D*.

2. *Guaiacum Test.*—Mix in a test-tube equal volumes of tincture of guaiacum and old turpentine which has become strongly ozonized by the action of air under the influence of light. To this mixture, which must not have any blue color, add the urine to be tested. In the presence of hæmoglobin, first a bluish green, and then a beautiful blue ring appears where the two liquids meet. On shaking, the mixture becomes blue. Normal urine, and albuminous urine, do not give this reaction. Urine containing pus also gives a blue color with the above reagents; but in this case the tincture of guaiacum alone, without the turpentine, is colored blue by the urine. The blue color produced by pus differs from that produced by hæmoglobin by disappearing on heating the urine to the boiling-point.

Urines, if alkaline from decomposition, must first be made faintly acid before applying this test. The turpentine should be kept exposed to the light, while the guaiacum should be kept in a dark-glass bottle.

3. *Heller's Test.*—If a neutral or faintly-acid urine containing hæmoglobin be heated to boiling, there is obtained a mottled precipitate of albumin and hæmatin. If caustic sodium be added to the boiling-hot test, the liquid becomes clear and turns green when examined in thin layers, and a red precipitate, appearing green by reflected light, re-forms, which consists of earthy phosphates and hæmatin.

FIBRINURIA.

Fibrin is a whitish, stringy solid when fresh, but upon drying it becomes of a grayish color. It is feebly soluble in 6-per-cent. solutions of potassium nitrate, in 5- to 15-per-cent. solutions of sodium chloride, in 5- to 10-per-cent. solutions of magnesium sulphate; and in solutions of other neutral salts, such as sodium sulphate and ammonium sulphate, most readily at a temperature of 40° C. It is insoluble in water, alcohol, and ether. It swells up in weak hydrochloric-acid solutions (0.2 per cent.), and also in caustic sodium or potassium solutions (0.2 per cent.), into a gelatinous mass. Stronger acids slowly dissolve fibrin with the formation of acid albumin (syntonin) and albumoses.

Digestive ferments act readily on fibrin. Thus, pepsin in an acid solution and trypsin (from the pancreas) in an alkaline solution cause, in the first place, a splitting up of the fibrin into two globulins, one coagulating at 56° C., the other at 75° C. Then the formation of albumoses and peptones follows.

Fibrin separates on the so-called spontaneous coagulation of the blood, lymph, and transudations.

Clinical Significance.—Fibrin may appear in the urine from various causes, either in solution or in coagulated flakes or masses. In the urine fibrin constitutes the basis of the so-called coagulable urine, which, upon standing some time, forms the fibrinous coagula. The quantity of fibrin present in the urine determines the extent of coagulation; sometimes only a sticky sediment forms at the bottom of the vessel; more rarely the coagulation involves the whole volume of urine, converting it into a sticky, gelatinous mass. This form of fibrinuria is seldom met with in the United States, but it occurs frequently as a special form of disease in Brazil and the Isle of France.

Fibrinuria, as it occurs with us, uniformly indicates that an exudation of fibrinous fluid—blood-plasma—has gained access to some part of the urinary tract. In most cases it comes from the kidneys, although it may result from intense inflammation of the lower urinary passages. It is often associated with hæmorrhages into the urinary tract, and it has been observed frequently in cases of villous tumors of the bladder.

It is important to distinguish between fibrinuria and those cases of pyuria in which large quantities of pus are present in highly-alkaline urine. In cystitis of long standing the ammonium carbonate resulting from bacterial decomposition of the urine may form with pus a gelatinous, sticky mass, which may be readily mistaken for fibrin coagulum. Such a urine, however, is thinned by the addition of water, and, moreover, if treated with acetic acid, a white precipitate falls, consisting of alkaline albuminate.

Detection.—The coagulum should be separated by filtration and washed with water, when it will show the following characters:—

1. It does not dissolve in water, but it swells up in 1-per-cent. solutions of hydrochloric acid, and is only dissolved when pepsin is added.

2. Separate the coagula from the urine by filtration through fine muslin, and wash with cold water. Treat a part of the mass with dilute solution of sodium hydroxide; if insoluble upon long standing, the indication is that it is fibrin, since albuminous bodies dissolve in sodium-hydroxide solutions. Treat another portion of the mass with a 1-per-cent. solution of sodium carbonate. Fibrin dissolves completely in this solution if warmed gently several hours on a water-bath. This solution is then filtered and treated with Millon's reagent, when a deep-red color is produced.

MUCINURIA.

Mucin, being the essential constituent of mucus, is, therefore, present in all urines, normal and abnormal; though in the urine of health the amount present is so minute as ordinarily to escape observation and elude all but the most delicate testing. Mucin is a proteid closely allied to the albumins, and may be made to yield albuminates and albumoses by boiling with dilute mineral acids. It is mucin that gives to the saliva, bile, and synovial fluids their peculiar, ropy consistency. The general features of the formation of mucin by mucous cells, and especially the behavior of the mucous granules in relation to the secretory activity of the submaxillary gland,[1] strongly indicate that mucin is derived from the true albumins; and, moreover, it yields many of the characteristics of proteids (Millon's and xanthoproteic reactions), and, as already noted, with mineral acids albuminates may be obtained. Our knowledge of mucin, however, as yet may be said to be in a somewhat transitional condition, since recent investigations render it probable that mucins derived from different sources are distinct substances, as are the different forms of albumins. Notwithstanding these facts, all mucins, from whatever source derived, possess certain features in common,—viz., they are non-coagulable by heat, soluble in alkalies and strong mineral acids. They are precipitated by strong alcohol and organic acids, as well as by dilute mineral acids. The presence of mucin in the urine, when in excess, constitutes one of the most frequent sources of error in searching for small quantities of albumin, as already shown. (See tests for albumin.)

Clinical Significance.—Mucin occurs in the urine in increased quantity in catarrhal inflammations of the urinary passages, more especially of the bladder. In cystitis and pyelitis the mucin in the urine is often very excessive, forming ropy, tenacious strings, and even sometimes settling in a jelly-like mass. Irritation of the urinary passages without inflammation or the formation of pus often causes a notable increase of mucin in the urine. An increase is also common in various febrile conditions, as pneumonia, pleuritis, typhoid fever, intermittent fever, pulmonary and intestinal catarrhs. It is of special interest to note, in this connection, as Reissner has pointed out, that in the beginning of the febrile state mucin often appears in the urine. A few days later albumin is often present; the latter usually disappears, after a longer or shorter time, while the mucin continues some days longer. Cases may be considered rare, according to Reissner, in which notable quantities of mucin in the urine persist for many days, under febrile conditions, without the appearance of albumin also. These facts should especially be borne in mind in scarlatina and the acute infectious fevers most often followed by nephritis, since, under such circumstances, the presence of mucin in the urine in marked quantities may serve to put the physician upon his guard against the approach of serious complications involving the kidneys.

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[1] Langley, Journal of Physiology, vol. x, 1889, p. 433.

Detection.—First dilute the urine with water, partly to prevent precipitation of uric acid on the subsequent addition of acid, and more especially to diminish the solubility of mucin by the sodium chloride of the urine. Next add an excess of acetic acid. The precipitate formed is mucin, and may be purified by dissolving in water, by the addition of a little alkali, and reprecipitating with acetic acid.

To distinguish between mucin and albumin in urine which gives proteid reactions, add to a column of urine three inches in depth in an ordinary test-tube about 1 drachm of potassium-ferrocyanide solution (1 in 20); after thorough mingling of these, add 10 to 15 drops of acetic acid. If precipitation occur, albumin, and not mucin, is present. Next test as described above for mucin, and in presence of precipitation mucin, and not albumin, is present.

SECTION IV.

CARBOHYDRATES.

The carbohydrates resemble one another in their chemical composition, in all containing 6 atoms of carbon, or a multiple thereof. They also resemble one another in their chemical characters, being neutral in reaction, not prone to enter into combinations, and, with the exception of inosite, they all possess a strong rotatory power over polarized light.

A number of carbohydrates are met with in the urine,—viz., glucose, levulose, lactose, inosite, etc.,—but the chief clinical interest with regard to this class of compounds at present belongs to grape-sugar.

Glycosuria.

Grape-sugar, or dextrose, in its pure form crystallizes in rhombic tablets, is soluble in its own weight of water, and gives a dextro-rotatory power over polarized light of $= + 56°$ (Hoppe-Seyler). Its solutions become brown when boiled with liquor potassæ, but with picric acid a deep mahogany red. In alkaline solutions it reduces salts of silver, bismuth, mercury, and copper; with the first three the metal is precipitated, cupric being reduced to cuprous compounds, with separation of cuprous oxide. Faintly-alkaline solutions of grape-sugar, colored blue by indigo, when boiled exhibit a beautiful color reaction, beginning with violet and ending in yellow. With solutions of sodium acetate it reduces phenylhydrazin hydrochloride to phenylglucosazone, forming highly characteristic and beautiful, golden-yellow, acicular crystals.

Grape-sugar exists in minute quantity in normal blood, varying chiefly with the functional activity of the liver. In some abnormal states of the system the amount of sugar in the blood becomes markedly increased, reaching its maximum—about $\frac{1}{10}$ per cent.—in the more pronounced diabetic conditions.

The ardently-disputed question if sugar be present in normal urine seems to have been conclusively settled in the affirmative through the researches of Wedenski (see Section II), although this is by no means universally conceded. Clinically speaking, this question is one of minor importance, since, if sugar be present in normal urine, it exists in such exceedingly minute quantity that it is unrecognizable by the ordinary methods of testing, and such quantities give rise to no marked clinical symptoms.

Clinical Significance.—Glycosuria may appear as a *temporary* condition in the course of a number of diseases, as cholera, intermittent fever, scarlatina, gout, cerebro-spinal meningitis, diseases of the lungs, liver, and the brain, especially if involving the fourth ventricle or vicinity. The administration of certain drugs and toxic substances causes the appearance of sugar in the urine, such as curare, carbonic oxide, amyl nitrite, methyl-delphinin, morphine, chloral, hydrocyanic acid, sulphuric acid, mercury, alcohol, strychnine, salicylic acid, turpentine, uranium nitrite, benzol, acetone, and phloridzin. Recent investigations have shown, however, in some of these cases, that the toxic agent merely causes the appearance of reducing agents[1] in the urine other than sugar.

Glycosuria may be produced experimentally by various lesions, as follows: By puncture of the floor of the fourth ventricle of the brain; injury to the vermiform process of the cerebellum; section of the spinal cord in different locations; destruction of various sympathetic ganglia; section of the splanchnic nerves; irritation of the vagus; section and stimulation of the central end of large motor nerves, as the sciatic; and by total extirpation of the pancreas in dogs. In addition to these, experimental glycosuria may be induced by measures which cause increased determination of blood to the liver, as by tying the accessory branch of the portal vein in animals, irritation of the liver by needle-punctures, compression of the aorta, etc.

Glycosuria in mild form may occur from disorders of the stomach, and, in some cases, the overingestion of starchy and saccharine foods will cause the appearance of sugar in the urine.

Glycosuria, however, of pronounced and *persistent form* belongs to the province of diabetes mellitus, and may always be regarded as symptomatic of grave defects either in the brain, liver, or pancreas. In young subjects the disease is almost uniformly progressive toward a fatal termination in from a few months to four or five years, notably so with patients under 20 years of age. During the middle period of life the disease is often less severe and less fatal. After the age of 50 it is often mild and amenable to treatment. Persistent glycosuria is the most constant and certain of all the symptoms of diabetes mellitus, being, in fact, sometimes the only symptom of the disease, and herein lies its great value for diagnostic purposes. It, therefore, becomes highly essential to be able to readily detect the presence of sugar in the urine, since diagnostic data of the most positive nature often hinges upon this point alone.

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[1] Usually glycuronic acid.

Detection of Sugar in the Urine.—The most popular method of searching for sugar in the urine has, heretofore, been by means of the copper tests. These all depend upon the fact, already noted, that in strongly-alkaline solutions grape-sugar reduces cupric oxide to lower grades of oxidation.

1. *Trommer's Test.*—This test may be conveniently performed as follows: About 1 drachm of urine, in an ordinary test-tube, is first treated with sufficient cupric-sulphate solution to render the urine a light-green color; then an equal volume of liquor potassæ is added. At first a blue precipitate of hydrated cupric protoxide results, which dissolves upon shaking the tube, forming a beautiful, clear, blue solution. If allowed to stand half an hour or so, reduction gradually takes place, especially if much sugar be present, resulting in precipitation of yellow or yellowish-red suboxide of copper. If, instead of standing half an hour, gentle heat be applied, this test becomes more delicate, and reduction, moreover, occurs at once.

This test is open to two objections: (*a*) If it be not submitted to boiling it is not very sensitive, only detecting sugar when present in considerable quantity. (*b*) If boiled especially long the test is rendered oversensitive, so that reaction may occur with substances in the urine other than sugar. The power of reducing cuprous oxide in alkaline solutions is possessed, to a feeble degree, by a number of substances[1] in both normal and abnormal urine, and in Trommer's test the quantity of urine submitted to the copper solution is relatively large, which greatly increases the chances of reduction by non-saccharine agents.

2. *Fehling's Solution.*—This solution is prepared according to the original standard formula, as follows: 34,639 grammes pure crystallized cupric sulphate; solution of sodium hydroxid (specific gravity, 1.12), about 500 cubic centimetres; chemically pure neutral sodium tartrate, 173 grammes. Prepare by dissolving the copper sulphate in 100 cubic centimetres of distilled water; next dissolve the neutral sodium tartrate in the caustic-sodium solution, and add the copper solution, little by little; finally, with distilled water bring the volume of the whole to 1000 cubic centimetres (1 litre).

Fehling's test may be applied as follows: Fill an ordinary test-tube to the depth of about an inch with the test solution, and raise to the boiling-point over a spirit-lamp. If upon boiling the solution remain clear blue, 3 or 4 drops of the suspected urine should be added, at the same time continuing the boiling; and if much sugar be present after a short interval, the solution suddenly assumes a dense, opaque, yellow color, and shortly after a yellowish-red sediment falls to the bottom of the test-tube. If no such reaction occur, the addition of urine may be continued until its volume equals, but *must not exceed*, the volume of the test; then, if no yellowish precipitate appear upon boiling, the urine may be considered free from sugar.

The chief objection to Fehling's solution is its well-known tendency to decompose upon keeping, so that it must be freshly prepared in order to be depended upon. Various methods have been proposed for the purpose of rendering this test stable. Thus, Dr. Pavy suggested having the solid ingredients compressed into pellets, the cupric salt and sodium tartrate being in separate pellets. In the author's experience these pellets are even more unstable than the liquid form of the test. The defect in Fehling's solution depends upon its contained sodium tartrate,

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[1] Chiefly uric acid, creatin, creatinin, hippuric acid, hypoxanthin, tannin, carbolic acid, alkaloids, and glycuronic acid.

—a very unstable salt; and so long as this be retained a portion thereof will be converted into racemic acid, which reduces cuprous oxide and corrupts the test.

3. *Haines's Test.*—The best form of copper test for sugar, qualitatively, is that devised by Prof. Walter S. Haines, of Chicago. The original formula for this test is as follows: Pure cupric sulphate, 30 grains; pure glycerin, 4 drachms; caustic potassium (in sticks), 3 drachms; distilled water, to 6 ounces. The solution is prepared by dissolving the cupric sulphate and glycerin in part of the water and the caustic potash in the remainder. Mix the two solutions.

For purposes of greater convenience, Professor Haines has recently simplified this formula, as follows: Take pure copper sulphate, 30 grains; distilled water, ½ ounce; make a perfect solution, and add pure glycerin, ½ ounce; mix thoroughly, and add 5 ounces of liquor potassæ.

In testing with this solution, take about 1 drachm and gently boil it in an ordinary test-tube. Next add from 6 to 8 drops—*not more*—of the suspected urine, and again gently boil. If sugar be present, a copious yellow or yellowish-red precipitate is thrown down. If no such precipitate appear, sugar is absent. This test is stable, and, though kept on hand indefinitely, it may always be depended upon to be in order for testing.

With regard to the copper tests in general: It has often been stated that if albumin be present in the urine it must first be removed, as it interferes with the reduction of the cupric oxide. In the author's experience, this rule may ordinarily be disregarded, except in the case of the bismuth test. With regard to boiling, it is important to bear in mind that, if this be continued too long, slight reduction is apt to occur with the urine, even when free from sugar, as evidenced by a slight *greenish* (not yellow) opacity; about half a minute should constitute the usual limit of boiling. It should also be borne in mind that strongly alkaline solutions are apt to precipitate the earthy phosphates of calcium and magnesium of normal urine in the form of a grayish cloud, which should not be mistaken for sugar.

4. *The Fermentation Test.*—This test depends upon the fact that grape-sugar is decomposed in the fermentation set up by

yeast, yielding alcohol, carbon dioxide, succinic acid, and a number of other products, with resulting decrease in the specific gravity of the urine. The following is the method employed: Fill an ordinary test-tube half full of mercury and the remaining half with the urine to be tested, and introduce into the urine a small piece of German yeast. Next close the mouth of the test-tube with the thumb and invert over a small vessel of mercury, and set aside in a warm room for several hours. If sugar be present fermentation proceeds at once, liberating the carbonic-acid gas which collects in the upper end of the tube, displacing the urine and mercury more or less, according to the quantity of sugar present. One precaution should be observed. Some specimens of yeast spontaneously evolve gas, and it is, therefore, best to perform a parallel experiment with yeast mixed with water, so that the spontaneously evolved gas may be estimated.

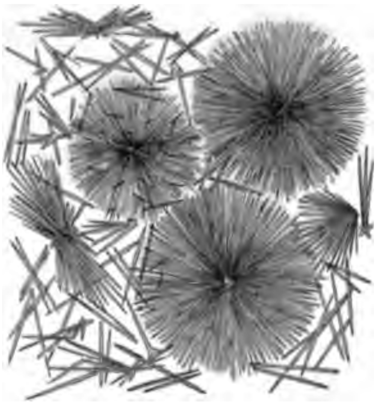
This test will detect sugar, if present in considerable quantity,—1 per cent. and over,—but the capacity of the urine itself for absorbing carbonic gas renders this test uncertain in detecting smaller quantities of sugar. The more serious disadvantage of this test for practical work is the fact that it requires several hours to complete the analysis.

5. *The Bismuth Test.*—Sugar possesses the power of reducing bismuth salts with resulting black precipitate, and upon this fact Bottger first suggested the following simple test: First add to the urine an equal volume of liquor potassæ and then a little basic nitrate of bismuth. Gently boil the whole, and if sugar be present the test turns gray or black, according to the amount of sugar present.

Traces of sulphur, which are often present in the urine, cause the same reaction with this test as does sugar. For the above reason, albumin, if present, must be removed before applying this test.

In order to eliminate the errors due to the presence of sulphur, Brucke suggested the following improvement of the bismuth test: Fill a test-tube half full of the suspected urine and another with a similar volume of water, and stand them side by side. To the one containing water add hydrochloric acid

PLATE II.



Crystals of Phenylglucosazone.
(After v. Jaksch.)

until a drop of Frohn's reagent[1] no longer produces a cloudiness. By this means an approximate estimation may be made of the quantity of hydrochloric acid which should be added to the urine. Acidify the urine with such quantity of hydrochloric acid, add the reagent, and filter. The filtrate, which should now remain clear upon adding hydrochloric acid, or the reagent, should be boiled with an excess of caustic potassium or sodium, as in Bottger's method; and if a gray or black color result, sugar is present.

6. *Phenylhydrazin Test.*—This test, suggested by Fischer, depends upon the power, possessed by phenylhydrazin hydrochloride, of forming with grape-sugar a highly-characteristic crystalline compound, termed *phenylglucosazone.* The best method of applying this test is as follows: To 25 cubic centimetres of suspected urine add 1 gramme of phenylhydrazin hydrochloride, 0.75 gramme of sodium acetate, and 10 cubic centimetres of distilled water in a capsule. The capsule should be placed in a water-bath and warmed at least an hour, then removed and allowed to cool; and if sugar be present even in minute quantity, there forms a yellowish deposit, which may appear amorphous to the naked eye, but which, when examined under the microscope, is seen to contain fine, bright-yellow, needle-like crystals, either single or in stars,—*phenylglucosazone*,—which melt at 204° C. (Plate II). The presence of small or large yellow scales or powerfully refracting brown spherules must not be taken for evidences of sugar, as only the bright-yellow, needle-like crystals are conclusive.[2]

If the mixture be left in the water-bath for a shorter time than an hour, a crystalline glycuronic-acid compound is formed (melting-point, 150° C.), which is likely to be mistaken for phenylglucosazone. For the same reason the method of boiling the reagents with the urine in a test-tube for only half a minute and cooling, as has been recommended by some, is apt to be misleading.

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[1] Frohn's reagent is prepared by mixing 1.5 grammes of freshly-precipitated bismuth subnitrate with 20 grammes of water, heated to boiling; then 7 grammes of potassium iodide and 20 drops of hydrochloric acid are added.

[2] In manipulating the phenylhydrazin hydrochloride caution should be observed not to get it on the hands, as it often causes troublesome eczema of very acute grade.

This test gives very trustworthy results with every variety of morbid urine, and is therefore equally applicable whether albumin be present or not. It gives no reaction with uric acid, urates, creatin, creatinin, oxybutyric acid, urochloralic acid, uroxanthic acid, tannin, morphine, salicylic acid, or carbolic acid.

A number of other tests have been proposed for the detection of sugar in the urine, among which may be mentioned: Boiling with sodium or potassium hydroxid (Moore), picric acid (Johnson), acetate of lead and ammonium (Rubner), alpha-naphthol and thymol (Molisch), indigo carmine (Mulder), bichloride of tin (Maumene), chromic acid (Hunefeld), diazo-benzol-sulphonic acid (Penzoldt), and sulphuric acid (Runge). None of the above tests possess special advantages over those already described, while, on the contrary, most of them are greatly inferior.

In addition to these, tests for sugar are prepared in paper form, by charging chemically-inert filtering-paper with sodium carbonate and indigo carmine. The chief merit of these papers is their portability, since they are neither sensitive nor trustworthy in detecting sugar in the urine.

Testing for Sugar in the Urine.—In searching for sugar in the urine, a test should, if possible, be selected which is simple in application, reasonably trustworthy, and perfectly stable, so that it may be depended upon when required, in routine work. In these respects Haines's test is very satisfactory.

Before submitting the urine to reagents always thoroughly cleanse all of the utensils to be employed in the analysis. In the use of the copper tests, *always employ a minimal amount of urine at first, gradually increasing until reaction is obtained or the stated limit of urine be reached.* This method greatly diminishes the chances of reduction by other substances in the urine than sugar, and, moreover, it gives a rough idea of the quantity of sugar when present. Thus, if Haines's test be selected, after gently boiling a drachm of the solution, add 2 or 3 drops of urine; then wait a moment, to see if reduction occur, before adding more urine, meantime continuing the boiling; if no reaction occur after a few seconds, add 2 or 3 more drops of urine, and so on until 8 drops be added, *but no more.*

If Fehling's solution be employed, gently boil a drachm of the test and, if it remain clear, add but a few drops of the suspected urine; then pause for a moment, continuing the boiling, and, if no reaction occur, add a few more drops of urine, and so on. If no reaction occur, continue the addition of urine until the volume thereof equals that of the test solution, *but not more.*

If any doubts arise as to the presence of sugar in the suspected urine, after the application of a routine test, an appeal should be made to one or more of the others described. For such purpose the phenylhydrazin test is desirable above all others, both because of its exceeding delicacy and its property of reacting with few known substances in the urine other than grape-sugar.

Determination of Sugar in the Urine.—Having detected the presence of sugar in the urine, it becomes all important to determine its quantity in all cases, because (*a*) such knowledge furnishes the most precise evidence of the grade and severity of the diseased state upon which it depends; (*b*) it furnishes the most solid basis upon which to construct the prognosis; (*c*) it gives the most trustworthy evidence as to the results of treatment.

1. *The Fermentation Method.*—The best results are reached with this test after the method suggested by Roberts.[1] It has already been stated that grape-sugar is decomposed in the fermentation set up by yeast, yielding alcohol, carbon dioxide, and a number of other products, with resulting *decrease in the specific gravity* of the urine. Each degree of specific gravity lost in fermentation corresponds to 1 grain of sugar per fluidounce. Thus, if before fermentation the specific gravity of the urine be 1.040, and after fermentation it be 1.020, it will have contained 20 grains of sugar per ounce. The method advised by Roberts is as follows: About 4 ounces of saccharine urine are put into a 12-ounce bottle, and a lump of German yeast is added to it.

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[1] Edinburgh Monthly Journal, October, 1861.

The bottle is then corked with a nicked cork (which permits the escape of the carbonic acid) and set aside, in a warm place, to ferment. Beside this is placed a tightly-corked 4-ounce bottle, filled with the same urine, but without any contained yeast. In about twenty-four hours the fermentation will have ceased. The fermented urine is then decanted into a urine glass and its specific gravity is taken; at the same time, the density of the unfermented urine in the companion bottle is observed and the *density lost* ascertained. The degrees of density lost represent the number of grains of sugar in each fluidounce of the urine tested. The percentage may be approximately ascertained by multiplying the number of degrees lost by 0.23.

The chief objection to this method for clinical work is the fact that it requires from eighteen to twenty-four hours to complete the analysis.

The *fermentation saccharometer* recently devised by Einhorn collects and measures the carbonic-acid gas evolved in fermentation, and from the volume of gas evolved the percentage of sugar is estimated. The urine itself absorbs carbonic-acid gas in quantity about equal to its own volume, and this gas the instrument takes no note of. The results obtained by these instruments are only approximative, and, in the author's experience, much less accurate than those obtained by Roberts's method of differential density.

2. *Fehling's Test.*—This is conducted by the titration method with Fehling's standard solution, the formula of which has already been given. The principle of the process depends upon the fact that, in the reduction of cupric oxide in solutions of definite strength by grape-sugar, the blue coloration disappears by the addition of a definite quantity of the sugar. Thus, with Fehling's solution every 10 cubic centimetres correspond to 0.05 gramme of grape-sugar,—or 200 grains to 1 grain of sugar. The test may be conducted as follows: Measure off 10 cubic centimetres of Fehling's solution in a glass flask and dilute with 3 or 4 volumes of water. The urine to be analyzed should be diluted to a known degree—ordinarily 1 to 10—unless the quantity of sugar be very small, in which case 1 to 5 is a better dilution. Next, raise the diluted Fehling's solution

to the boiling-point, and, after having filled the burette with the diluted urine, add the latter in successive small amounts to the boiling Fehling's solution until the blue color has entirely disappeared. After each fresh addition from the burette, the mixture should be gently boiled and then allowed to stand for a few seconds, so that the yellow suboxide of copper may subside and the observer may see whether the mixture contains any blue color. As soon as the blue color has disappeared the quantity of diluted urine employed may be read off, and since it takes just 0.05 gramme of sugar to remove the blue coloration in the 10 cubic centimetres of copper solution, from this the percentage of sugar in the urine may be readily reckoned. Thus, if 10 cubic centimetres of the diluted urine were required, this would represent 1.2 cubic centimetres of urine, which would contain 0.05 gramme of sugar. The number of grammes of sugar contained in 100 cubic centimetres of urine would be obtained by proportions, thus:—

$$\frac{1.2}{0.05} = \frac{100}{x} \therefore x = \frac{100 \times 0.05}{1.2} = 4.16$$

The objection to Fehling's standard solution, already noted, —viz., its instability,—greatly detracts from its practical utility. In addition to this, in quantitative testing its end reaction is defective; so that some practice is necessary in order to determine the precise point of reduction.

Dr. Pavy improved the end reaction of the copper test for quantitative work by the addition of ammonium to his formula. Unfortunately, however, he retained the sodic tartrate, which renders his solution equally unstable with Fehling's solution. Neither of these solutions will keep sufficiently long to make them available for practical use.

It has recently been proposed to alter Fehling's solution by substituting 175 cubic centimetres of pure glycerin for the sodic-tartrate and 130 grammes of potassium hydroxid for the caustic-sodium solution. The author finds, however, that this renders the end reaction of Fehling's solution still more defective, since the cupric suboxid formed in presence of the potassium base is less dense than with sodium, and therefore is more bulky and

takes a longer time to settle; so that it is very difficult to find the precise point of reduction. Furthermore, a more serious consequence of this proposed alteration of Fehling's formula is the fact that in changing the alkaline base of the test from sodium to potassium it also changes the ratio of reduction of the cupric oxide by sugar; so that the proposed formula would, in testing, indicate considerably more sugar in the urine than is actually present. The ratio of reduction of cuprous oxide by sugar varies with the form of alkaline base employed. Thus, with sodium hydroxid (as in Fehling's solution) the ratio is 1 grain of sugar to 6.92 grains of cupric sulphate; while with potassium hydroxid it is 1 grain of sugar to 6.66 grains of cupric sulphate. Fehling's solution, therefore, cannot be altered by changing its alkaline base and still retain any accuracy as a quantitative test for sugar according to its original ratio of reduction.

3. *The Author's Method.*—In view of the fact that the determination of sugar in the urine had never been rendered entirely satisfactory for practical every-day work, the author, about four years since, devised the following formula,[1] with the object of eliminating the defects of the copper test for quantitative work, and also for bringing out the best results of the titration method. The four years' subsequent use of this test justifies its recommendation for the uses for which it was designed.

The formula for the author's standard solution is as follows: Cupric sulphate (C. P.), 4.742 grammes; potassium hydroxid (caustic potash) (C. P.), 23.50 grammes; strong ammonium (U. S. P.) (sp. gr. 0.9), 450 cubic centimetres; glycerin (C. P.), 38 cubic centimetres; distilled water, to 1000 cubic centimetres (1 litre).

Prepare by dissolving the cupric sulphate and glycerin in 200 cubic centimetres of distilled water with the aid of gentle heat. In another 200 cubic centimetres of distilled water dissolve the caustic potassium. Mix the two solutions, and when cold add the ammonium. Finally, with distilled water bring the

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[1] The formula has since been improved and standardized in both the metric and English systems of weights and measures.

Haines Sol with NaH

NaHO H	16.90	4.22
CuSO4	4,566	1.142
NH O-aq	450 cc	
Glycerin	38	10
Aq ad	1,000	250

35cc = .020 Glucose

For 500 cc

NaHO	8.45 gm
CuSO4	2.283
Glycerin	20.
Aquae ad	500 cc

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lution are reduced
gramme) of grape-

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FIG. 9.—THE AUTHOR'S APPARATUS FOR QUANTITATIVE DETERMINATION OF SUGAR IN URINE.

Proceed by accurately measuring 35 cubic centimetres of the solution into the flask, dilute with about 2 volumes of distilled water, and bring the whole *thoroughly* to the boiling-point. Fill

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[1] It is important that the glycerin be chemically pure. The ammonium should be U. S. P. strength, sp. gr. 0.9; that sold as chemically-pure, strong ammonia-water is best.

[2] Messrs. E. H. Sargent & Co., 108 Wabash Avenue, Chicago, prepare and keep in stock the above solution, as well as the apparatus required for testing.

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takes a longer time to settle; so that it is very difficult to find the precise point of reduction. Furthermore, a more serious consequence of this proposed alteration of Fehling's formula is the fact that in changing the alkaline base of the test from sodium to potassium it also changes the ratio of reduction of the cupric oxide by sugar; so that the proposed formula would, in testing, indicate considerably more sugar in the urine than is actually present. The ratio of reduction of cuprous oxide by sugar varies with the form of alkaline base employed. Thus, with sodium hydroxid (as in Fehling's solution) the ratio is 1 grain of sugar to 6.92 grains of cupric sulphate; while with potassium hydroxid it is 1 grain of sugar to 6.66 grains of cupric sulphate. Fehling's solution, therefore, cannot be altered by changing its alkaline base and still retain any accuracy as a quantitative test for sugar according to its original ratio of reduction.

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[1] It is important that the glycerin be chemically pure. The ammonium should be U. S. P. strength, sp. gr. 0.9; that sold as chemically-pure, strong ammonia-water is best.

[2] Messrs. E. H. Sargent & Co., 108 Wabash Avenue, Chicago, prepare and keep in stock the above solution, as well as the apparatus required for testing.

3. *The Author's Method.*—In view of the fact that the determination of sugar in the urine had never been rendered entirely satisfactory for practical every-day work, the author, about four years since, devised the following formula,[1] with the object of eliminating the defects of the copper test for quantitative work, and also for bringing out the best results of the titration method. The four years' subsequent use of this test justifies its recommendation for the uses for which it was designed.

The formula for the author's standard solution is as follows: Cupric sulphate (C. P.), 4.742 grammes; potassium hydroxid (caustic potash) (C. P.), 23.50 grammes; strong ammonium (U. S. P.) (sp. gr. 0.9), 450 cubic centimetres; glycerin (C. P.), 38 cubic centimetres; distilled water, to 1000 cubic centimetres (1 litre).

Prepare by dissolving the cupric sulphate and glycerin in 200 cubic centimetres of distilled water with the aid of gentle heat. In another 200 cubic centimetres of distilled water dissolve the caustic potassium. Mix the two solutions, and when cold add the ammonium. Finally, with distilled water bring the volume of the whole to exactly 1000 cubic centimetres (1 litre).[1] Thirty-five (35) cubic centimetres of this solution are reduced upon boiling by exactly 2 centigrammes (0.02 gramme) of grape-sugar.

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[1] The formula has since been improved and standardized in both the metric and English systems of weights and measures.

The analysis should be conducted as follows: Have on hand a glass flask (150 to 200 cubic centimetres' capacity), a common retort-stand, a 10-cubic-centimetre or 20-cubic-centimetre graduated burette, and a large spirit-lamp.[2]

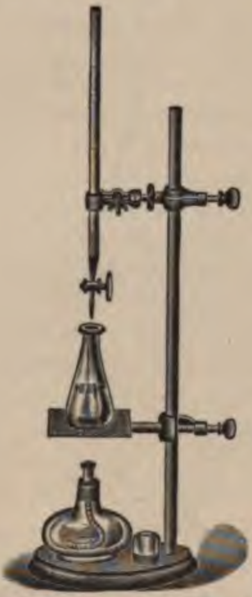

FIG. 9.—THE AUTHOR'S APPARATUS FOR QUANTITATIVE DETERMINATION OF SUGAR IN URINE.

Proceed by accurately measuring 35 cubic centimetres of the solution into the flask, dilute with about 2 volumes of distilled water, and bring the whole *thoroughly* to the boiling-point. Fill

the burette to the zero-mark with the urine to be tested, and *slowly discharge* the urine into the *boiling* test solution drop by drop, until the blue color begins to fade; then *still more slowly*, three to five seconds elapsing after each drop, until the blue color completely disappears and leaves the test solution perfectly *transparent and colorless*.[1]

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[1] It is important that the glycerin be chemically pure. The ammonium should be U. S. P. strength, sp. gr. 0.9; that sold as chemically-pure, strong ammonia-water is best.

[2] Messrs. E. H. Sargent & Co., 108 Wabash Avenue, Chicago, prepare and keep in stock the above solution, as well as the apparatus required for testing.

The number of cubic centimetres it requires to discharge the blue color in 35 cubic centimetres of the test solution contain exactly 2 centigrammes (0.02 gramme) of sugar.

The following, therefore, is the percentage relationship of reduction of the test:—

If 35 cubic centimetres of the test solution be reduced by 2 cubic centimetres of urine, there is exactly 1 per cent. of sugar; reduced by 1 cubic centimetre, 2 per cent.; reduced by ¾ cubic centimetre, 3 per cent.; reduced by ½ cubic centimetre, 4 per cent.; reduced by ¼ cubic centimetre, 8 per cent.

If absolute accuracy of results be desired, it is better to dilute the urine to be tested with 2 volumes of distilled water and divide the product by 3, especially if the percentage of sugar be high.

Those who prefer to work with the English weights and measures may obtain the same accuracy of results by using the following formula and methods:—

Sulphate of copper, C. P.,	44 grains.
Caustic potash, C. P.,	214 grains.
Strong ammonia, U. S. P. (sp. gr. 0.9),	9 fluid ounces.
Glycerin, C. P.,	6 drachms.
Distilled water,	to 20 ounces.

Prepare by dissolving the sulphate of copper and glycerin in 4 ounces of distilled water, with the aid of gentle heat. In another 4 ounces of distilled water dissolve the caustic potash. Mix the two solutions, and when cold add the ammonia. Finally, with distilled water bring the volume of the whole to exactly 20 fluidounces.

Ten drachms of the above solution are reduced upon boiling by exactly $\frac{1}{3}$ grain of grape-sugar. The test is conducted precisely as already described in the metric system, save that a minim burette is substituted for the cubic-centimetre burette and the result is reckoned in grains instead of grammes.

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[1] It will be noted after testing, that upon standing some time the test solution resumes the blue color again. This is due to absorption of oxygen from the atmosphere, which reforms the blue protoxide of copper from the cupric suboxide held in solution by the ammonium. This should not be mistaken for imperfect reduction or defect in the test solution.

To determine the number of grains of sugar per ounce in any given sample of urine, divide 480 (the number of grains per ounce) by the number of minims it required to discharge the blue color in 10 drachms of the test solution; divide the product by 3 and the result is the number of grains per ounce.

Example.—If 16 minims of urine reduce 10 drachms of the test solution, there are 10 grains of sugar per ounce,—

$$\frac{480}{16} = \frac{30}{3} = 10 \text{ grains of sugar.}$$

If it be desired to know the percentage amount of sugar present, divide the number of grains per ounce by 4.8.

The advantages claimed for the above test are as follow: 1. Its perfect end reaction, whereby even the inexperienced observer may accurately determine the precise point of complete reduction without delay. 2. Its stability, which is such that the solution may be kept on hand for months without impairment of its qualities for testing. 3. Its rapidity of application, by means of which one is enabled to determine the quantity of sugar in a given sample of urine within five minutes. 4. Its accuracy, which any one may readily prove by submitting to it solutions of grape-sugar *in normal urine* of known and accurately-measured strength. 5. Its simplicity, the apparatus required being of the most common order.

4. *Optical Saccharimetry.*—As already stated, grape-sugar possesses a right rotatory power over polarized light, and upon this fact has been based a method of quantitative testing for sugar by the polariscope. Among the more elaborately-constructed instruments for this purpose are those of Lippich, Misterlich, Soleil, Laurent, Wild, and von Flieschel.

Ultzmann has devised a polarizing saccharimeter, which possesses several important advantages over the instruments named, as follows: (*a*) No artificial light is needed, for the concave mirror of the microscope-stand brilliantly illuminates the field of vision. (*b*) The apparatus itself is small, scarcely longer than the elongated tube of the ordinary microscope, and needs no separate stand. (*c*) By means of this instrument the percentage of sugar can be directly calculated. (*d*) The entire apparatus can be had for a comparatively small cost.

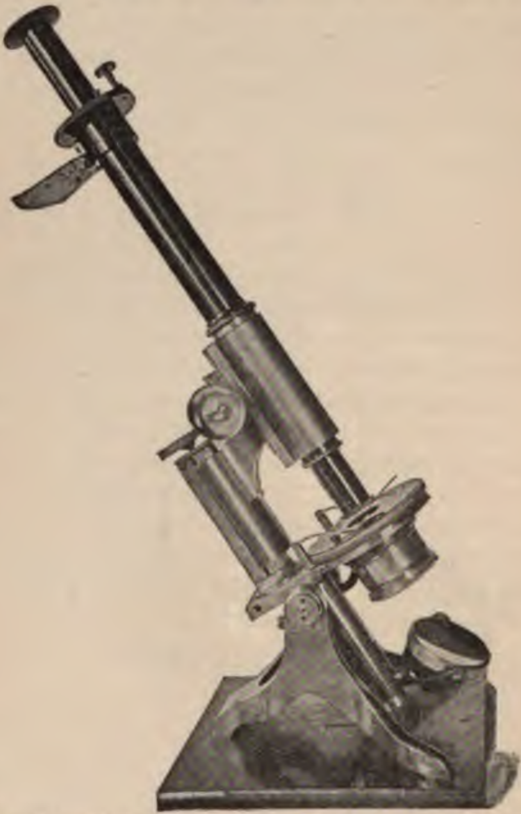

FIG. 10.—ULTZMANN'S POLARIZING SACCHARIMETER ADJUSTED TO MICROSCOPE-STAND.

In using this saccharimeter, the tube, objectives, and ocular of the microscope are removed, and in their place the saccharimeter is inserted and made fast by means of a small screw. The concave mirror is then adjusted, and, by looking through the instrument, it is determined whether or not it is properly adjusted.

In Fig. 11 *a* is the biconcave and *b* the objective lens of a small Dutch telescope, the focal distance of which extends to *p*; *c* is the upper Nicol prism, with which a vernier is closely connected; *d* is a glass tube for holding the suspected fluid, which should be filtered or otherwise cleansed before analysis; *p* is a double plate of right and left rotating quartz, and *f* the lower Nicol prism.

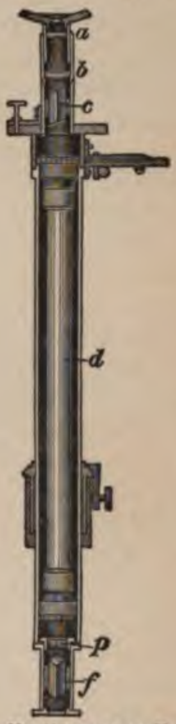

FIG. 11.—SECTIONAL VIEW OF ULTZMANN'S POLARIZING SACCHARIMETER.

The arc or fixed scale is so divided that one division of it represents 1 per cent. of grape-sugar at a temperature of 20° C. By means of the vernier, *tenths of a degree (i.e., of 1 per cent.)* can be approximately determined. Since 10 degrees of the vernier correspond exactly with 9 degrees of the arc, to the percentage of sugar found must be added as many tenths as spaces are counted on the vernier up to that division which exactly coincides with a division of the arc.

If, for example, the zero-point of the vernier does not quite reach (toward the right) the 5-point of the scale, it indicates that the percentage of sugar is more than 4 and less than *5 per cent.* If it be desired to estimate *the tenths per cent.*, and the *sixth* division of the vernier is the first (counted from the zero-point) to coincide with a division of the arc, then 6 is the number of *tenths* required, and the apparatus would indicate, in this case, 4.6 per cent. grape-sugar present. In estimating the strength of cane-sugar solutions, it is to be borne in mind that the polarization power of cane-sugar is three-fourths that of grape-sugar.

Cane- and grape- sugar, as well as lactose, turn the polarized ray to the right, while albumin and levulose, on the other hand, turn it toward the left. If the glass tube of the saccharimeter be empty, or contain a fluid holding in solution substances having no optical influence (as normal urine), the zero-point of the vernier coincides exactly with the zero-point of the scale, and the two halves of the field of vision are exactly isochromatic. If, on the contrary, an optically-active substance be contained in the fluid,—as, for example, sugar,—the normal isochromatism of the two halves disappears, and a distinctly unequal coloring takes place. This is the more apparent the greater the amount of optically-active substance present in solution. When this unequal coloring occurs the vernier is to be moved toward the right or left (according to the presence of sugar or albumin) until the color of the two halves is again exactly the same. The percentage is then read off the scale in the way above mentioned.

If a diabetic urine be very light colored and clear, it can at once be put into the glass tube of the instrument and the determination made. If, however, it be dark and cloudy, and contain albumin, it is advantageous to first clarify it and remove all disturbing substances. This is best accomplished by means of a 10-per-cent. aqueous solution of sugar of lead. The lead acetate causes in urine a copious white precipitate, consisting of lead chloride, phosphate, and sulphate, and the precipitate carries down with it all the coloring matter of the urine and such albumin as may be present. If the urine be then passed through a dry filter, the resulting filtrate is almost as clear as water, and is particularly well adapted for the apparatus. Since, however, the amount of sugar in the mixture (after the addition of the lead-acetate solution) differs from that in the urine, the amount of dilution must be taken into account in estimating the sugar present. It is best, therefore, to take 75 cubic centimetres of urine, and to that add 25 cubic centimetres of lead-acetate solution, shake, and filter. In estimating the sugar present in the urine, one-quarter of the percentage of the mixture added to that percentage will give the percentage of sugar in 100 cubic centimetres of urine. In other words, the percentage of the mixture is three-quarters that of the urine. Thus, if to 75 cubic centimetres of a dark, albuminous, saccharine urine have been added 25 cubic centimetres of lead-acetate solution, the mixture filtered, and found to contain 4.8 per cent. sugar, then 1.2 per cent. must be added to give the percentage in 100 cubic centimetres of urine, which would, therefore, contain $4.8 + 1.2$ per cent. $= 6$ per cent. sugar. In filling the glass tube care must be observed that no air-bubbles are included in the fluid. It is well, therefore, to fill the tube as full as possible and push the glass cover on from one side before screwing down the cover (Ultzmann).

The author uses this instrument, obtaining fairly rapid and satisfactory results if the quantity of sugar be over 1 per cent., but in quantities much less than this the results are uncertain.

LEVULOSURIA.

Fruit-sugar, or levulose, has been found in the urine of persons whose symptoms correspond closely with those of diabetes mellitus. In such cases the levulose may be associated with grape-sugar, or it may appear alone, but usually the former is the case.

Levulose turns the plane of polarization to the left, and this fact enables us to distinguish it from grape-sugar, which turns it to the right. Levulose reduces copper salts as does grape-sugar, although more feebly than the latter. It also yields the characteristic reaction of yellow crystallization with phenylhydrazin hydrochloride, but these crystals melt at 150° C., while those formed from grape-sugar require a temperature of 204° C. to melt them. Levulose does not crystallize, and does not melt so readily as does grape-sugar. When cane-sugar is treated with dilute mineral acids, it undergoes a process known as inversion, —*i.e.*, it takes up water and is converted into a mixture of equal parts of dextrose and levulose.

Clinical Significance.—Aside from the fact that levulose is sometimes found in the urine in diabetic conditions, either alone or, as is more common, in association with grape-sugar, little else is known of its clinical relations. It has been stated that excessive ingestion of cane-sugar, as well as the sugars of certain kinds of fruits, may cause the appearance of levulose in the urine, more especially in conditions of disturbed digestion. This, however, is rather conjectural than the result of observation, although cane-sugar is converted in the intestines into glucose and levulose.

Detection.—If saccharine urine deflect polarized light strongly to the left, we may infer that the saccharine substance is levulose. If other known substances which turn polarized light to the left be excluded, it may be regarded as certain that levulose is present.

LACTOSURIA.

Lactose, or milk-sugar, crystallizes in white, rhombic prisms, which are soluble in 6 parts of cold and 2½ parts of hot water. It has only a faintly-sweet taste, and is insoluble in alcohol and ether. Aqueous solutions of lactose possess a right, or dextro-rotatory, power over polarized light of + 59.3°, and do not readily undergo alcoholic fermentation. It reduces the copper salts upon boiling in alkaline solutions, but about one-third less powerfully than does grape-sugar. If long boiled with dilute acids, it forms *galactose*, which, treated with nitric acid, yields *mucic acid.*

Clinical Significance.—Lactose occurs frequently in the urine of women who are nursing, the quantity usually being small, although it may reach as high as 3 per cent., and be attended by all the usual symptoms of diabetes, as in a case reported by Ralfe, at the London Hospital. In this case the woman was suffering from debility, and lactosuria occurred after three successive confinements, the urine being free from sugar during the gestation.

Lactose is nearly always present in the urine of women two or three days after confinement, and just before milk appears in the mammary glands (during milk fever); and the same may be said of women within a day or two after weaning their children. Lactosuria may also arise from any cause that prevents the milk escaping from the mammary glands during lactation, such as inflammations involving the mammary ducts.

Detection.—If urine give the characteristic reaction of grape-sugar with alkaline solutions of cupric salts, and if it also cause extreme deflection of the polarized ray to the right, it is probable that lactose is present. Confirm by treating the urine with an excess of lead acetate, filter, and to the filtrate add ammonium until a permanent precipitate forms. The fluid is then heated, but not boiled; and if a rose-red color gradually develop, which slowly vanishes on standing, grape sugar is present; if no such reaction occur, lactose is present (Rubner).

INOSITURIA.

Inosite, or muscle-sugar, crystallizes in large, colorless, monoclinic prisms, sometimes grouped in rosettes. They are soluble in 6 parts of water at 20° C., insoluble in alcohol and ether. Inosite does not undergo alcoholic fermentation, and possesses no rotatory power over polarized light. It does not reduce alkaline solutions of cupric salts, although it gives with them a greenish tint upon boiling, which clears up on standing, and again turns green on boiling.

Although termed muscle-sugar, inosite has been found in the lungs, spleen, liver, kidneys, and brain, and it has been found in the urine in a number of pathological conditions.

Clinical Significance.—Inosituria has frequently been noted in association with diabetic conditions. It has also been observed in typhus, phthisis, syphilitic cachexia, and in diseases of the medulla. In a number of cases of inosituria Ralfe observed moderate polyuria, loss of flesh, general malaise, and aching in the limbs, although no tangible disease could be made out. Inosituria not infrequently takes the place of glycosuria, especially in the milder grades of diabetes or in convalescence from the latter. Inosituria is also occasionally associated with albuminuria in Bright's disease. Gallois found inosite in the urine of 7 out of 102 patients examined. Of these, it occurred 5 times in 30 cases of diabetes and in 25 cases of albuminuria.

Detection.—1. If a solution of inosite be evaporated with a little nitric acid on platinum almost to dryness, and the residue be moistened with a little ammonium and solution of calcium chloride, and the mixture again be evaporated carefully to dryness, a vivid rose-red or violet color arises, which is apparent with even 1 milligramme of inosite (Scherer). Other sugars do not give this reaction.

2. Add a little mercuric nitrate solution[1] to a solution of inosite on a porcelain dish; a yellow precipitate is produced. On heating this gently it will become red; on cooling the color vanishes, but re-appears again on gently heating. Uric acid, urea, starch, lactose, mannite, glycocoll, tannin, cystin, and glycogen do not give this reaction. Albumin is colored red and grape-sugar black, and therefore, if present, these should be removed.

3. Inosite may be isolated from the urine, as follows: After first removing the albumin, if present, the urine is treated with neutral lead acetate until precipitation ceases. It is then filtered and the warmed filtrate treated with subacetate of lead as long as any precipitate occurs. It is well to concentrate the urine to one fourth of its bulk before precipitation. The lead precipitate containing the inosite combined with lead oxide is collected after twelve hours, and, after washing, is suspended in water and decomposed with sulphuretted hydrogen. A little uric acid first separates upon standing awhile; the fluid is separated therefrom by filtration and the filtrate concentrated by boiling, and is treated with three or four volumes of alcohol while boiling. A heavy precipitate results, and the hot alcoholic solution is poured off, unless the precipitate be flocculent and non-adhesive, in which case it may be filtered through a heated funnel and allowed to cool. If, after twenty-four hours, inosite crystals have deposited, as is usual, in groups, they are filtered and washed with cold alcohol. If, however, no crystals of inosite have separated, ether is added to the clear, cold, alcoholic filtrate until a milky cloudiness results upon standing, and it is then allowed to stand in the cold for twenty-four hours. If too little ether has not been employed, almost all of the inosite present is separated in the form of shining, pearly leaflets.

ALLIED SUBSTANCES OCCASIONALLY FOUND IN URINE.

GLYCURONIC ACID.

This substance is closely allied to carbohydrates, its formula being $C_6H_{10}O_7$. When pure it is not crystalline, but its anhydride forms colorless, acicular crystals. It is insoluble in ether, but soluble in water and hot alcohol, crystallizing out from the latter on cooling. Though so closely related chemically to the carbohydrates, it yields, with urea, decomposition products of an aromatic nature, as orthonitrobenzyl alcohol. It occurs in the urine as a potassium salt, $C_6H_9O.K$. Bromine converts glycuronic acid into saccharic acid, indicating its close relationship to dextrose, as well as to the aldehyde group. It has been thought to arise from dextrose in the organism, though Kulz suggested its origin to be from inosite.

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[1] Prepared by dissolving 1 part of mercury in 2 parts of nitric acid, and evaporate to one-half and add 1½ parts of water. After twenty-four hours, pour the clear fluid from the basic salt.

Glycuronic acid, of all substances met with in the urine, is most likely to be mistaken for grape-sugar, since it gives a heavy yellow or even red precipitate with cuprous oxide, reduces bismuth, silver, and mercury salts, and is dextro-rotatory.

Significance.—Glycuronic acid occurs in the urine abundantly after the administration of such drugs as chloral and butyl-chloral, nitrobenzol, camphor, curare, morphia, chloroform, etc., in consequence of which it was formerly thought that the use of these substances caused the appearance of grape-sugar in the urine. It sometimes, though not frequently, occurs in the urine of people who are apparently in good health and are not diabetic; so that it is important to distinguish between this condition and glycosuria.

Detection.—1. If the urine reduce cupric oxide and is dextro-rotatory, but fails to undergo alcoholic fermentation with the yeast test, glycuronic acid is present. 2. It may be isolated from the urine by the method of Schmiedeberg and Mayer, as follows: A large quantity of urine is decolorized by animal charcoal, evaporated to a syrup, and then digested with large quantities of damp barium hydrate in the presence of gentle heat over a water-bath. It is then extracted with absolute alcohol; glycuronic acid and other substances are left undissolved. The residue is mixed with water and filtered; more baryta is added to the filtrate; it is again filtered, and the filtrate evaporated down over a water-bath. An amorphous barium compound separates out; this is washed with water, decomposed by sulphuric acid; the barium sulphate is filtered off, the filtrate is evaporated down and dried *in vacuo*, when crystals of the anhydride will be obtained.

CANE-SUGAR.

After abundant use of cane-sugar as food, traces of it may be found in the blood and sometimes in the urine. Pure cane-sugar possesses no reducing power over cupric oxide; but as met with commercially it sometimes contains other sugars as impurities, which may cause slight reduction of the copper tests.

Cane-sugar crystallizes in monoclinic prisms, aqueous solutions of which possess strong dextro-rotatory powers $+ 73.8^\circ$. By boiling with water, or more readily with dilute mineral acids, it undergoes inversion,—*i.e.*, it takes up water and separates into dextrose and levulose. Nitric acid oxidizes cane-sugar into saccharic acid.

Detection.—It has been stated that if cane-sugar be boiled some time in water it undergoes inversion, becoming glucose and levulose. With solutions of cane-sugar the polarization is dextro-rotatory, but after inversion it becomes levulo-rotatory, because the left-handed action of the molecule of levulose produced $= -106^\circ$ is only partly neutralized by the right-handed action of the glucose $= +56^\circ$.

GLYCOGEN.

This substance is found in the liver, muscles, placenta, white blood-corpuscles, cartilage-cells, pus-cells, and in embryonic tissues. It has also been found in the urine, notably in some diabetic conditions. Pure glycogen is a snow-white, amorphous powder, tasteless and odorless, soluble in water, insoluble in alcohol and ether. Glycogen is strongly dextro-rotatory $+211^\circ$, but does not reduce cupric oxide. Glycogen gives with iodine a port-wine red color; the color disappears on heating, and re-appears on cooling.

SECTION V.

ABNORMAL URINE (*continued*).

ACETONURIA.

Acetone—C_3H_6O—is a thin, watery, colorless liquid, of specific gravity 0.792, which boils at 56.5° C., and possesses a peculiar ethereal or fruit-like odor. It may be obtained in considerable quantity by distillation of the urine as well as the blood of diabetic patients. Acetone is also sometimes found in the urine of children apparently in good health.

Heated with potassium iodide and caustic potassium, iodoform is evolved; with solutions of nitroprusside of sodium and ammonium a rose-red color is produced.

Acetone and aceto-acetic acid are sometimes both present in the urine, sometimes only one of them. V. Jaksch holds that acetone is a normal constituent of urine, though occurring in minute quantity (0.1 gramme in twenty-four hours). On the other hand Le Noble holds that acetone only occurs in healthy urine after the use of alcohol or foods rich in proteids. Both acetone and aceto-acetic acid seem to be decomposition products of albumins.

Clinical Significance.—Acetonuria of pronounced degree often accompanies high febrile states, probably caused by blood changes which result from exalted temperatures, since acetonuria belongs to no special form of fever. Moreover, the amount of acetone in the urine in febrile conditions corresponds closely with the degree of temperature elevation, always rising and falling with the latter.

Acetonuria often occurs in diabetes mellitus, more especially in advanced cases. In such cases it sometimes precedes the more dangerous symptom of diaceturia. Acetonuria is frequently associated with certain forms of cancer, notably carcinoma. It is also observed in cases of inanition or starvation and in cerebral psychosis, especially if accompanied by great mental excitement. Acetonuria may result from excessive use of animal foods, and this may, in a measure, account for its frequent appearance in diabetes, since such patients are usually restricted largely to nitrogenous diet. A condition of auto-intoxication with acetone sometimes occurs, which is accompanied by acetonuria. This state gives rise to symptoms of restlessness, excitement, and even delirium, but unless accompanied by diaceturia it tends toward a favorable termination (Jaksch), although it may end in coma and death in some cases.

Acetonuria occurs in association with the following diseases: Small-pox, typhus, pneumonia, scarlet fever, measles, Bright's disease, perityphlitis, and strangulated hernia, but it is never accompanied or followed by diabetic coma in such cases.

Detection.—1. *Lieben's* iodoform test, as modified by Ralfe, is as follows: 20 grains of potassium iodide are dissolved in a drachm of liquor potassæ and boiled; the urine is then floated upon the surface of the fluid in a test-tube. At the point of contact a precipitation of phosphates occurs, which, if acetone be present, becomes yellow and studded with yellow points of iodoform.

A more delicate method of application of this test is to first distill a small quantity of the urine, and apply the test to the distillate. This test has one disadvantage: lactic acid and ethyl alcohol behave with it similarly to acetone.

2. *Chautard's Test.*—A drop of aqueous solution of magenta decolorized by sulphurous acid gives, with fluids containing over 0.01 per cent. of acetone, a violet color. This appears in dilute solutions after four or five minutes.

3. *Le Noble's Test.*—On adding an alkaline solution of sodium nitroprusside—so dilute as to have only a slight red tint—to a fluid containing acetone, a ruby-red color is produced, which in a few minutes changes to yellow, and on boiling, after adding acid, to greenish blue or violet. A quarter of a milligramme of acetone can be thus detected.

4. *Baeyer's Indigo Test.*—A few crystals of nitrobenzaldehyde are dissolved by heat in the suspected urine; on cooling the aldehyde separates in the form of a white cloud. The mixture is thus made alkaline with dilute sodium solution, and, if

acetone be present, first yellow, then green, and lastly an indigo-blue color will appear within ten minutes.

5. *Reynolds's Test.*—This test depends upon the fact that acetone promotes the solution of mercuric oxide. The test may be conducted as follows: The yellow precipitate of mercuric oxide, obtained by the reaction of mercuric chloride with an alcoholic solution of caustic potassium, is added to a small quantity of the urine, which is shaken and filtered. To the clear filtrate ammonium sulphate is carefully added, and if acetone be present some of the mercuric oxide is dissolved and a black ring of sulphide of mercury appears at the plane of contact between the two liquids.

DIACETURIA.

Diacetic or ethyl-diacetic acid ($C_6H_{10}O_3$) is a colorless, strongly-acid liquid which mixes with water, alcohol, and ether in all proportions. On heating to boiling with water, especially with acids, diacetic acid decomposes into carbon dioxide and acetone. It differs from acetone in giving a violet-red or brownish-red mahogany color with solution of ferric chloride. This color decreases at ordinary temperatures within twenty-four hours, and more rapidly upon boiling, in which respects it differs from phenol, salicylic acid, acetic acid, and sulphocyanides.

Diacetic acid has frequently been confused with and mistaken for acetone. Under the influence of alkalies it takes up water and splits into acetone, alcohol, and carbonic acid:—

$$C_6H_{10}O_3 + H_2O = C_3H_6O + C_2H_6O + CO_2.$$

If this take place in the blood or urine, it is probably the sodium salt which undergoes similar decomposition:—

$$\underset{\text{Sodium-ethyl diacetate.}}{C_6H_9NaO_3} + 2H_2O = \underset{\text{Acetone.}}{C_3H_6O} + \underset{\text{Alcohol.}}{C_2H_6O} + \underset{\text{Sodium-hydrogen carbonate.}}{NaHCO_3}.$$

This view of the origin of acetone is supported by the fact that alcohol is often found in the urine at the same time. There are, it is true, other substances in the urine at times which give, under certain circumstances the ferric-chloride reaction,—viz., β-hydroxybutyric acid, sulpho- (thyo-) cyanates, acetic acid, and formic acid; and, according to Legal and Hammarsten, the urine of patients who have taken thallin, antipyrin, salicylic acid, and carbolic acid may give the reaction. If, however, as already stated, the urine be previously boiled, diacetic acid still gives the ferric-chloride reaction, while the other substances do not. Fleischer found that the substance which gives the ferric-chloride reaction in the urine is not taken up by ether after the urine is acidulated with sulphuric acid, whereas diacetic acid is soluble in ether. Salkowski confirmed this observation, and found, moreover, that the urine, after boiling, did not give the ferric chloride reaction. These last-named observers hold that in most cases it is not diacetic acid from which acetone originates, but some at present unknown substance, possibly hydroxybutyric acid already mentioned (Halliburton).

Clinical Significance.—Diaceturia is always pathological, and, for the most part, it may be regarded as a symptom of serious import. It is of least serious significance when occurring, as is not uncommon, in febrile conditions in children. Under such circumstances recovery usually follows. In the case of adults it is always of more grave significance. In diabetes the occurrence of diaceturia may be looked upon as the almost certain prelude to coma, which usually terminates quickly in death. Von Jaksch, indeed, considers that diabetic coma is due to the presence of diacetic acid in the blood, and he, therefore, proposes to substitute the term *diacetic coma* for the former name.

Diaceturia is most common in the advanced stages of diabetes, and more especially in young subjects of the disease. It does not, apparently, depend upon large quantities of sugar in the urine, at least directly so, since the appearance of diaceturia is often preceded by decided diminution of sugar.

It sometimes occurs at the height of acute fevers, and in adults such occurrence is of grave significance.

Diaceturia is sometimes the index of auto-intoxication—*diacetæmia*—and is accompanied by such symptoms as vomiting, dyspnœa, jactitation, which shortly ends in coma and death without other discoverable disease or lesion.

Detection.—This is best accomplished by v. Jaksch's method, as follows: Take a recently-voided sample of urine, and add a few drops of ferric-chloride solution thereto. If the phosphates be precipitated filter them off, and to the filtrate add a few drops more of ferric-chloride solution. If a red color is produced, boil a portion of the urine, and to another portion add a few drops of sulphuric acid and shake with ether. If the red color appear but slightly or not at all in the boiled portion, and grows pale after twenty-four hours in the ethereal extract, and, furthermore, acetone be detected in considerable quantity in the distillate, diacetic acid is present.

CHOLURIA.

The biliary acids and pigments are the chief bile-elements of clinical interest met with in the urine.

BILIARY ACIDS.

It is an unsettled question as yet if the bile-acids occur in the urine under physiological conditions. According to Vogel, Dragendorff, Hone, and Oliver, traces of bile-acids occur in normal urine, although Hoppe-Seyler and Udransky hold the opposite view. Oliver's new and delicate method of testing for the bile-acids gives his results much weight, and it may be assumed that the evidence is in favor of the view that the bile-acids are present in minute quantities in the urine of health.

Clinical Significance.—Dr. Oliver estimates the amount of bile-salts in normal urine as about 1 part in from 10,000 to 15,000 parts. Furthermore, in a series of observations he has noted that the normal percentage quantity varies with the time of day, reaching the maximum during periods of fasting, as in the morning urine and that passed before meals; while it quickly diminishes after meals, reaching the minimum about three hours after food. Dr. Oliver also observed an increase of the bile-acids in the urine upon active muscular exertion; and he suggests that changes of temperature, atmospheric pressure, use of alcohol, etc., also influence the degree of discharge of the bile-salts by the kidneys. The bile-salts in the urine are markedly augmented in all forms of jaundice, and, moreover, according to Oliver's observations, this occurs both before the appearance of the bile-pigments and long after their disappearance from the urine.

In so-called acute bilious attacks—*i.e.*, biliary engorgement from defective bile excretion—there appears to be an overflow of the bile-elements into the blood, accompanied by such symptoms as feeble pulse, pallor, coldness of the extremities, sensations of chilliness, slow respiration, nausea and vomiting, with headache, and sometimes diarrhœa. During these symptoms the bile-salts in the urine are at first diminished, but after a time they are increased, and thereupon immediate relief from these symptoms follows.

Acute cholæmia from retention of bile-salts in the blood may pass beyond the ordinary bilious attack and produce the more serious symptoms of lowered temperature, convulsions, albuminuria, with evidences of blood dissolution such as hæmoglobinuria.

Hepatic congestion, early cirrhosis, and malarial poisoning are accompanied by increased elimination of the bile-acids in the urine, more especially if accompanied by constipation. Dr. Oliver has noted excess of the bile-acids in the urine in carcinoma, amyloid disease, enlargement of the liver, cirrhosis, and in hepatic tumors. Choluria always follows a rise of temperature, and in high fevers the increase of bile-acids may reach 400 per cent. above the normal range. In splenic leucocythæmia, anæmia, hæmoglobinuria, and scurvy a large excess of the bile-acids appears in the urine. Lastly, Dr. Oliver has noted a decided and persistent decrease of the bile-acids in the urine in cases of chronic interstitial nephritis,—granular kidney.[1]

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[1] In view of the fact that nearly all advanced chemico-physiologists are now agreed that the liver constitutes the chief agent of destruction of those substances which we know to be auto-intoxicants to the organism, Dr. Oliver's explanation of the hepatic origin of certain symptoms seems to the author vastly more reasonable than the explanation of many of the same symptoms by Haig's uric-acid theories. The author has searched in vain among the classic experiments of Bouchard, as well as others, for proof that uric acid is in any way toxic to the organism, even when injected into the blood in the enormous dose of 0.64 gramme per kilogramme of body-weight. On the other hand, the bile-salts are toxic in almost infinitesimal doses; they are not only toxic, but in aqueous solutions of 2 per cent. *they kill* 1 kilogramme of weight; the cholate of sodium in dose of 54 centigrammes, and cholate of potassium in dose of 46 centigrammes. The enormous toxic power of bile, as a whole, may be judged from the following statement of Bouchard as a result of direct experimentation: "We must conclude that during twenty-four hours a man makes, by the activity of his liver alone, enough poison to kill three men of his own weight."

Detection.—1. Pettenkoffer's method is as follows: The urine is mixed with concentrated sulphuric acid, taking care that the temperature does not rise higher than 60° to 70° C. Then a 10-per-cent. solution of cane-sugar is added drop by drop, continually stirring with a glass rod. The presence of bile-acids is indicated by the production of a beautiful red liquid, the color not disappearing at ordinary temperature, but becoming more bluish violet in the course of a day or so. This red liquid shows a spectrum with two absorption bands, the one at *F* and the other between *D* and *E* near *E*.

This test fails if the solution be heated too high or an improper quantity—usually too much—sugar be added. In the last case the sugar carbonizes and the test becomes dark brown or brown. The reaction fails if the sulphuric acid contains sulphurous acid or the lower oxides of nitrogen. Since many other substances, such as albumin, oleic acid, amylalcohol, morphine, give a similar reaction; in doubtful cases the spectroscopical examination must not be omitted.

If the urine be icteric and of pronounced color, the bile-acids must first be isolated from the urine by Hoppe-Seyler's method before applying the above test, as follows: Strongly concentrate the urine and extract the residue with strong alcohol. The filtrate is freed from alcohol by evaporation and then precipitated by basic lead acetate and ammonium. The washed precipitate is treated with boiling alcohol, filtered hot, the filtrate treated with a few drops of sodium solution, and evaporated to dryness. The dry residue is extracted with absolute alcohol, filtered, and an excess of ether added. The amorphous or, after a longer time, crystalline precipitate, consisting of alkali salts of the biliary acids, may then be submitted to the above-described test.

2. *Dr. Oliver's method* of detecting the bile-acids is most sensitive and simple. The principle of this method depends upon the physiological fact that such products of gastric digestion as peptone and propeptone are precipitated in the duodenum by contact with the bile-acids. Therefore, since peptone in an acid solution, as the urine, is precipitated by the bile-acids or their derivatives as cholate of sodium,[1] an acid solution of

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[1] The form in which the bile-acids occur in the urine.

peptone may be used as a test for the bile-acids. The following is the formula for the test solution: Pulverized peptone (Savory and Moore's), ℥ss; salicylic acid, 4 grains; acetic acid, ℥ss; distilled water to 8 ounces. To be filtered repeatedly until rendered transparent. In testing, the urine must be perfectly cleansed, if not already so, and rendered acid if it be alkaline or neutral, and the specific gravity reduced to 1008 if it be above it. To 60 minims of the test solution 20 minims of the urine are added. If bile-acids be present in normal amount, there will be no immediate reaction visible, but shortly a slight tinge of milkiness will be produced. If in excess, a distinct milkiness at once appears, becoming more intense in proportion to the quantity of bile-acids present. On agitation the opalescence diminishes, and may even disappear, but it returns upon the addition of more of the test solution. On this fact is based an approximate quantitative test, for which is prepared a standard solution by adding equal parts of test fluid and normal urine diluted to specific gravity 1008. Any urine requiring 60 minims or more to bring its opacity up to that of the standard does not contain an excess of bile-acids.

DR. OLIVER'S STANDARD TABLE.

Urine.				Percentage Increase of Bile-Salts Over the Normal.	Urine.				Percentage Increase of Bile-Salts Over the Normal.
Minims.		Drops.			Minims.		Drops.		
1	or	2	=	6000	20	or	40	=	300
2	or	4	=	3000	25	or	50	=	240
3	or	6	=	2000	30	or	60	=	100
4	or	8	=	1500	35	or	70	=	83
5	or	10	=	1200	40	or	80	=	66
10	or	20	=	600	45	or	90	=	50
15	or	30	=	400					

Percentage increase over 700 above the normal is rarely encountered. With the above test Dr. Oliver detects 1 part of bile-salts in 18,000 or 20,000 parts of sodium-chloride solution. If careful attention be paid to details in preparation of the urine, nothing as yet found in urine interferes with the test.

BILIARY PIGMENTS.

Bile coloring matters appear in the urine in a number of conditions. The urine in such cases is always abnormally colored, —yellow, yellowish brown, deep brown, greenish yellow, greenish brown, or even nearly pure green. On shaking the urine it froths and the bubbles are yellow or yellowish green in color. The morphological elements of the sediment often take the color of the abnormal pigment in the urine.

Clinical Significance.—The biliary pigments are met with in the urine in jaundice, from whatever cause it arises, but most commonly, perhaps, when due to obstruction of the bile-ducts. In such cases the bile-elements make their way into the lymphatics and the general circulation and are eliminated by the kidneys. The bile-pigments appear in the urine several days before the icteric coloration of the skin is perceptible, and therefore they may sometimes be taken as a prognostic of the approach of jaundice.

The biliary coloring matters are also found in the urine in numerous pathological conditions of the liver, in which icterus may or may not be present also. They may also appear in the urine as a result of blood changes, and after hæmorrhage into the tissues; and in such cases they are derived from their primary source in the blood itself. Lastly, bile-pigments in large amounts always appear in the urine in cases of phosphorus poisoning.

Detection.—1. *Gmelin's method* consists in introducing a column of strong nitric acid, containing a little yellow nitrous acid of commerce ($HNO_3 + NO_2$) into a test-tube, and upon this gently floating a column of similar depth of urine. In the zone between the fluids appears from below upward the colors green, blue, violet, red, and yellow. The green is most predominant, while the blue is most indistinct or sometimes absent.

(*a*) In Rosenbach's modification of this test the urine is filtered through a fine, thick filter. After filtration a drop of nitric acid containing a little nitrous acid is applied to the inside of the filter. A pale-yellow spot will be formed, which is surrounded by colored rings which appear yellowish red, violet, blue, and green. This modification is very delicate, and it is hardly possible to mistake other coloring matters for the bile-pigments.

(*b*) Dragendorff has adopted still another modification of the above test, which consists in placing a little of the urine on a plaster-of-Paris disc, and, when nearly absorbed, a drop of nitric

Make HNO_3 by heating $NaNO_3$ with pieces of [illegible] wood – [illegible] use starch instead acid is allowed to fall on the moistened spot. If the bile-pigments be present a ring forms about the acid drop, in which green is predominant.

2. *Huppert's test* detects the faintest traces of bile-pigment in the urine. The urine is treated with lime-water, or first with some $CaCl_2$ solution, and then with a solution of sodium or ammonium carbonate. The precipitate, consisting of bile-pigments, may be shaken out with chloroform after washing in water, and after acidification with acetic acid. The bilirubin is taken up by the chloroform, which is colored yellow thereby, while the acetic-acid solution is colored green by the bilirubin.

The lime-pigments may also be used directly for Gmelin's test in the following way: Spread them on a porcelain dish in a thin layer, and add a drop of nitric acid. The reaction usually appears very beautiful.

3. *Ultzmann's test* consists in treating 10 cubic centimetres of the urine with 3 or 4 cubic centimetres of concentrated caustic-potash solution and then acidifying with hydrochloric acid. The urine will turn a beautiful green color if the bile-pigments be present.

INDOXYL-SULPHURIC ACID.

Indoxyl-sulphuric acid ($C_8H_7NSO_4$), also called *urine indican*, and formerly known as *uroxanthin*, occurs in normal urine as an alkali salt, whose properties have been fully considered in Section II Indoxyl-sulphuric acid is derived from indole, which is first oxidized in the system into indoxyl and then is united with sulphuric acid. Indole is formed by the putrefaction of proteids, and hence the quantity excreted by the kidneys is greater upon a meat than upon a vegetable diet.

Clinical Significance.—Variations in the quantity of so-called indican in the urine occur within comparatively narrow range in health; but in certain pathological conditions the increase becomes very marked. Clinically, therefore, an increased excretion of this substance by the kidneys is observed in Addison's disease, cholera, carcinoma of the liver, chronic phthisis, central and peripheral diseases of the nervous system, typhoid fever, dysentery, acute general peritonitis, multiple lymphoma, fetid bronchitis, ichorous pleural exudations, diabetes mellitus, as well as in a number of others.

In obstructive diseases of the small intestine its excretion is sometimes enormously increased, owing probably to the favorable conditions for the absorption of indole. The simple obstruction of the colon does not cause its increase in the urine. Obstruction of the large intestine, only when it causes considerable disturbance in the motion of the contents of the upper ileum, gives rise to its increased excretion by the kidneys.

In general, it has been considered that the appearance of large quantities of so-called indican in the urine implies that an abundant albuminous putrefaction is progressing in some part of the system. Thus, in pleurisy it indicates a copious, unhealthy exudation, and in peritonitis it may be taken as an evidence of the formation of unhealthy pus. The putrefaction of secretions rich in albumin in the intestines explains its increase in the urine during starvation.

Detection of Urine Indican.—*Jaffe's method* consists in mixing 10 cubic centimetres of strong hydrochloric acid with an equal volume of urine in a test-tube, and, while shaking, add drop by drop a perfectly fresh, saturated solution of chloride of lime, or chlorine-water, until the deepest obtainable blue color is reached. The mixture may next be titrated with chloroform, which readily takes up the indican and holds it in solution, and the quantity present may be approximately estimated according to the depth of the color. If the urine contain albumin it should be removed before applying this test, otherwise the blue color, often arising from the mixture of hydrochloric acid and albumin after standing, may prove misleading.

2. *MacMunn's Method.*—(*a*) Equal parts of urine and hydrochloric acid with a few drops of nitric acid are boiled together, cooled, and agitated with chloroform. The chloroform becomes violet if much indican be present, and shows an absorption band before *D*, due to indigo blue, and another after *D*, due to indigo red.

This method is more trustworthy than Jaffe's, because chloride of lime destroys small quantities of indigo.

(*b*) A rough, approximate method may be employed upon the foregoing principle, as follows: Pour 4 cubic centimetres of hydrochloric acid into a small flask, and while stirring add from 10 to 20 drops of urine. If the proportion of indican be about normal the resulting color will be rather light-yellow; if in excess the acid will turn violet or blue—the more intense will be the color in proportion to the quantity of indican present. If no coloration appear after waiting a minute or two the indican is not in excess, however deep a color may subsequently appear.

If 2 or 3 drops of nitric acid be added to the test, as in the original method, it becomes more delicate. (See also page 43.)

THE DIAZO REACTION IN URINE.

The diazo test was suggested by Ehrlich, in 1882, as a valuable diagnostic measure in typhoid fever, although he admitted the occurrence of this reaction in a few other conditions shortly to be considered.

The diazo reaction depends upon the fact that if sulphanilic acid (*amidosulphobenzol*) be acted upon by HNO_2, *diazosulphobenzol* is formed, which unites with certain aromatic substances occasionally present in the urine to form aniline colors.

Dr. Friedenwald has recently reviewed the literature of this reaction,[1] and shown that many of the contradictory results obtained by some observers are due to failure in carrying out Ehrlich's methods in performing the test, which is best accomplished as follows:—

To obtain diazosulphobenzol in a perfectly fresh condition, sulphanilic acid is kept in solution with hydrochloric acid; to this sodium nitrite is added, whereupon HNO_2 is liberated and diazosulphobenzol is formed.

Process.—Two solutions are prepared, as follows:—

1. Two grammes of sulphanilic acid; 50 cubic centimetres of hydrochloric acid; 1000 cubic centimetres of distilled water.
2. A 0.5-per-cent. solution of sodium nitrite.

In performing the test 50 parts of No. 1 and 1 part of No. 2 are mixed, and equal parts of this mixture and of the urine in a test-tube is rendered strongly alkaline with ammonium. If the reaction be positive the solution assumes a carmine-red color, which on shaking must also appear in the foam. Upon standing for twenty-four hours a greenish precipitate is formed.

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[1] New York Medical Journal, December 23, 1893.

The test must not be considered positive unless a distinct red coloration extends to and includes the foam on shaking.

Clinical Significance.—Ehrlich's original claims for the diazo reaction were as follow :—

"1. The reaction is most commonly found in typhoid fever from the fourth to the seventh day and thereafter, and if the reaction be absent the diagnosis is doubtful.

"2. Cases of typhoid fever characterized by faint reaction and occurring only for a short time may be predicted to be of very mild type.

"3. The reaction is occasionally noted in phthisis pulmonalis, but only in cases pursuing a rapid course toward a fatal termination.

"4. The reaction is sometimes, but not often, observed in cases of measles, miliary tuberculosis, pyæmia, scarlet fever, and erysipelas.

"5. In diseases unaccompanied by fever, as chlorosis, hydræmia, diabetes, diseases of the brain, spinal cord, liver, and kidneys, the reaction is always absent."

The weight of clinical evidence strongly confirms all of Ehrlich's original claims for this reaction, but more especially so with regard to typhoid fever and pulmonary tuberculosis; if present in the latter disease any length of time, the prognosis is very unfavorable.

β-Oxybutyric Acid ($C_4H_8O_3$).

This acid forms an odorless syrup which is readily miscible with water, alcohol, and ether. It is an optically active substance, being, in fact, dextro-rotatory; so that it interferes with the estimation of sugar in the urine by polarimetry. It is non-precipitable by lead acetate and ammoniacal basic lead acetate. On boiling with water in the presence of a mineral acid, it decomposes into *α-crotonic acid*—which melts at 72° C.—and water. It yields aceton upon oxidation with chromate mixture.

Clinical Significance.—The appearance of hydroxybutyric acid in the urine was first demonstrated by Minkowski, Kulz, and Stadelmann. It is usually accompanied by diacetic acid in the urine, and sometimes by aceton. It is especially noted in the urine in severe or chronic cases of diabetes mellitus. It has also been observed in the urine in cases of measles, scurvy, scarlet fever, and in diseases of the brain. Aside from these, little is at present known of its clinical relations.

Detection.—1. If a urine be dextro-rotatory after fermentation with yeast, it is strongly probable that hydroxybutyric acid is present. 2. *Kulz's method* consists in evaporating the fermented urine to a syrupy consistence, and, after the addition of an equal volume of concentrated sulphuric acid, distill directly without cooling; *α-crotonic acid* is produced, which is distilled, and, after strongly cooling, the distillate is collected in a glass; crystals which melt at + 72° C. separate. If no crystals be obtained, then shake the distillate with ether and test the melting-point with the residue, which has been washed with the water obtained after evaporating the ether.

PTOMAINES AND LEUCOMAINES.

The term *ptomaine* was originally used to designate those products of putrefaction which give the reaction of vegetable alkaloids and possess more or less poisonous characters. It has since been found that similar alkaloids are formed during the life of animal organisms; these are termed *leucomaines.* Ptomaines, or putrefactive bases, are transition products of decomposition; or, in other words, temporary forms through which matter is being transformed from the organic to the inorganic state by means of the action of bacterial life. They are chemical compounds of a basic nature, and their deep interest and importance in the field of modern medicine may at once be perceived from the fact that they constitute the chemical factors in the causation of all infectious diseases.

It has been erroneously supposed that all ptomaines are highly poisonous; but not only are many of them inert, but it may be stated that the majority of them isolated to date do not produce harmful results to the organism in ordinary quantities. On the other hand, some of them are highly toxic, and such Brieger first proposed to designate as "toxins."

Ptomaines resemble vegetable alkaloids in that they all contain nitrogen as the chief element of their basic character. Some of them also contain oxygen, corresponding to the vegetable fixed alkaloids, while those devoid of oxygen correspond to the volatile alkaloids.

Selmi was probably the first—in 1880—to claim that the basic substances formed in the organism during pathological changes often appeared in the urine, constituting an index to the pathological condition of the patient. He demonstrated, in the urine of a patient with progressive paralysis, two bases resembling *nicotine* and *coneine*. Since then Bouchard, Villiers, Lépine, Gautier, and others have demonstrated the presence of a few other basic products in the urine in other diseased conditions. It is now well known that the urine in certain diseases, as cholera and septicæmia, is decidedly toxic in character. Bouchard Chavrin, and Ruffer have proved that bacterial poisons generated in the system through disease can be excreted in the urine. They produced immunity to the action of the *bacillus pyocyaneus* upon animals by previous injections of urine of animals inoculated with that bacillus as well as with filtered cultures thereof. Unfortunately, as yet these investigations have not been pushed to sufficient completion to furnish much practical data in reference to infectious diseases, since but few bacterial ptomaines have yet been isolated from the urine. The importance, however, of this comparatively new field of uranalysis can scarcely be overestimated, since it is strongly probable that careful investigation of the urine in this direction may throw important light upon a large class of diseases.

It only remains here to refer to the few ptomaines which have been isolated from the urine, and the methods by which this has been accomplished. First, with regard to normal urine, much difference of opinion prevails as yet in reference to the presence or absence of alkaloidal toxins. When through defective renal action the leucomaines become retention products, they at once assume immense importance in the chemistry of the urine. The researches of Pouchet strongly confirm the presence of toxic alkaloids in normal urine; while, on the other hand, Villiers denied their existence, claiming that the observed physiological action is wholly due to the presence of potassium salts. Since we know that toxins of an alkaloidal nature (leucomaines) are formed in the organism through tissue metabolism, and, furthermore, that the urine constitutes at least one channel of escape for similar compounds, there seems no reason to doubt their presence in urine; at least, in minute quantity. Bouchard, Guerin, and Lépine have shown that at least that which has been taken for these compounds is greatly increased in the urine in pathological states.

With regard to the isolated ptomaines, Baumann and Udransky separated several basic derivatives, amongst them *cadaverin*, *putrescin*, and a small amount of a third base from the urine of a patient suffering from catarrhal cystitis; normal urine being found free from these substances.

Putrescin—$C_4H_{12}N_2$—is closely related to *cadaverin*, since they nearly always occur together or alternately from the same source. Brieger obtained it from putrefying human viscera after exposure of from three days to three weeks at ordinary temperatures. It has been obtained from herring (twelve days' exposure), from pike (six days' exposure), from haddock (two months' exposure), and from decaying mussel (sixteen days' exposure). It is especially abundant in cultivations of comma or cholera bacillus, and hence it is believed that substances similar to *putrescin* are the true chemical poisons in cholera. *Putrescin* has been isolated from the urine in cases of cystinuria by several observers since Brieger's first discovery. It is toxic to the organism, but its tetra-methyl derivation is incomparably more so, causing symptoms of salivation, dyspnœa, contraction of the pupils, muscular paralysis of the limbs and trunk, ejaculation of semen, dribbling of urine, and violent convulsions.

Cadaverin—$C_5H_{14}N_2$—appears in decomposing tissues usually before the occurrence of *putrescin*. Brieger obtained it from putrefying heart, liver, lungs, etc., at ordinary temperatures, in three days' exposure; from putrid mussel in sixteen days. Like *putrescin*, it is a constant product of comma bacillus upon any soil upon which they may be cultivated. *Cadaverin* is a constant associate—perhaps a product—of the activity of *vibriones*, since it never occurs in cultures in which this genus is absent. It is therefore absent from both normal and typhoid stools, as well as from cultures of the bacillus of Emmerich and Eberth. Both *putrescin* and *cadaverin* may be obtained from the urine of cystinuria by precipitation with benzoyl chloride (Baumann's method).

Trimethylamine—C_3H_9N—has been found in human urine. This base occurs both in animal and vegetable tissues. It has been obtained from ergot, the blood of calves, herring-brine, in the putrefaction of yeast, in cheese, in human liver and spleen (two to seven days' exposure), in perch (six days' exposure), in cultures of *streptococcus pyogenes* on broth and blood-serum. It is not a violent toxin, large doses being required to markedly disturb the system.

Beatin—$C_5H_{13}NO_3$—is a well-known base, the product of cotton-seed, beet-juice, turnip, vetch-seeds, etc. It has been found in the urine by Liebrich. This base is of no pathological significance, since it is non-toxic to the organism.

Jaksch, who has studied the subject of basic derivatives of the urine, both normal and pathological, finds that, while normal urine and that of some diseases hold these substances only in minute quantity, in certain other morbid states this amount is very considerable. He makes the following suggestions as a guide for investigation in this field of work :—

In the first place, he suggests that it would be well to follow the example of Brieger, Baumann, and Udrasky in withholding the name *alkaloids* from the bodies *diamines*, which are derived from the system under morbid conditions, because all that have been recognized as yet are simply *diamines*, and do not exhibit the characteristic property of alkaloids, viz., the pyridin radicle. In the second place, it is desirable to discriminate between the physiological bases of the urine creatinin, reducin, etc., which belong to normal urine, and those which are associated only with certain diseased states. It is not intended to imply by this that the physiological bases—*leucomaines*—cannot under any circumstances give rise to diseased or poisonous symptoms. On the contrary, it is highly probable that retention, and still more the increased formation of such products, under certain circumstances may induce very grave symptoms, and even greatly imperil the life of the patient. Again, it seems probable that in certain acute diseases, specific substances of a toxic nature, not present in normal urine, may be excreted with that fluid.

Jaksch makes the following suggestive classification of the subject :—

(*a*) Clinical (morbid) symptoms depending upon retention of the physiological basis. Under this head would come uræmia and certain of the symptoms of obstruction—*retention toxicosis*.

(*b*) Clinical symptoms referable to the presence of basic products which are found in the system (blood, etc.) in disease and eliminated with the urine—*noso-toxicosis*.

(*c*) Clinical symptoms which are caused by the formation of toxic basic substances from morbid matter, such as pathological fluids lodged in certain parts of the organism. Such bases being absorbed give rise to symptoms of severe poisoning. Under this head would come the collective symptoms of ammoniæmia, and others which follow the absorption of gangrenous pus—*auto-toxicosis*.

(*d*) Clinical symptoms, and consequently morbid types induced by the action of toxic bases taken into the system with the food, such as the poison of sausages, cheese, canned fruits, etc., etc.—*exogenic toxicosis*.

DETECTION.—A number of methods are in use for the detection and isolation of these bases, the more prominent of which are those of Dragendorf, Stas-Otto, Brieger, Gautier, and Etard. Since all of these methods are somewhat difficult and tedious, only the most suitable methods for uranalysis will here be described. For such purposes Brieger's method serves best; but in some cases it is important that the urine be first concentrated *in vacuo*. Sufficient hydrochloric acid is first added to render the urine acid, and the mixture is then boiled for a few minutes and filtered. The filtrate is concentrated at first over a flame, and subsequently over a water-bath, to a syrupy consistence.

In consequence of the instability of the bodies sought, it is advisable to evaporate *in vacuum* and at the lowest possible temperature, more especially so if the urine be foul.

The thick fluid is next mixed with 96-per-cent. alcohol, filtered, and the filtrate treated with a warm alcoholic solution of lead acetate. The resulting lead precipitate is removed by filtration and the filtrate concentrated—preferably *in vacuo*—to a syrup, and again taken up in 96-per-cent. alcohol. The alcohol is next evaporated, and the residue, dissolved in water, is freed from lead by the addition of sulphuretted hydrogen and filtration. The filtrate is acidified with hydrochloric acid and evaporated to a syrupy consistence. It is then diluted with alcohol, and alcoholic solution of mercuric chloride is added. The resulting precipitate is boiled in water, and certain ptomaines may separate at this stage in consequence of different solubilities of the double salts of mercury. The better to secure this, the precipitate may be treated successively with water at various temperatures. Should it be thought that the lead precipitate may have retained some of the ptomaines, it may be suspended in water, the lead converted into sulphide, and the fluid treated in the manner just described.

The solution obtained as above is filtered, freed from mercury, and evaporated; the excess of hydrochloric acid is carefully neutralized with sodium carbonate (the reaction is kept feebly acid), then it is again extracted with alcohol to free it from inorganic salts. The alcohol is evaporated, the residue dissolved in water, the remaining traces of hydrochloric acid neutralized with sodium, the whole acidified with nitric acid and treated with phosphomolybdic acid. The phosphomolybdate double compound is separated by filtration and decomposed by neutral lead acetate or, more readily, by heating over a water-bath. The lead is next removed by means of sulphuretted hydrogen (hydrogen sulphide); the filtrate is evaporated to a syrupy consistence and taken up with alcohol. Several ptomaines are thus separated as hydrochlorates, and may be obtained in the form of double salts of gold, or platinic chloride, and of picric acid. The chloride of the base is obtained by removing the metallic base by precipitation with sulphuretted hydrogen, while the picrate is taken up with water, acidified with hydrochloric acid, and repeatedly extracted with ether to remove the picric acid. The last step is to ascertain if any ptomaines remain in the phosphomolybdic-acid filtrate after precipitation of the phosphomolybdic acid.

Brieger has obtained some of his ptomaines by a simpler modification of his above complete method. Thus he has obtained *neurodin* by treating the aqueous extract of the organic matter, after boiling and filtration, with mercuric chloride, collecting the precipitate, decomposing it with sulphuretted hydrogen, evaporating the filtrate over a water-bath, and extracting the base with alcohol.

Properties of Animal Bases.—1. They all have an alkaline reaction.

2. They are insoluble in water; soluble in acids forming compounds; precipitated from such compounds by ammonium.

3. Iodine and potassium iodide give a brown, flocculent precipitate.

4. Potassio-mercuric-iodide solution produces flocculent, yellowish-white precipitates, insoluble in acids and dilute alkalies, easily soluble in alcohol, and generally, also, in ether.

5. Iodide of bismuth and potassium give orange precipitates in solution acidulated with dilute sulphuric acid.

6. Phosphomolybdic acid gives a bright or brownish-yellow precipitate, insoluble in water and dilute mineral acids.

7. Metatungstic and phosphotungstic acids give a white, flocculent precipitate, with difficulty soluble in water and dilute acids.

8. Tannin in neutral or feebly-acid solutions give yellow or white precipitates with most ptomaines.

9. Chloride of gold gives a yellow or yellowish-white precipitate, either amorphous or crystalline.

10. They are all oxidizable and unstable, especially under the influence of an excess of mineral acid, which colors them red and then converts them into a resinous mass.

11. Picric acid precipitates most of them, the color of the precipitate usually being pale yellow.

12. The animal bases are energetic reducing agents, decomposing chromic acid, iodic acid, and silver nitrate. With potassium ferrocyanide and ferric chloride they give Prussian blue. This was formerly considered to be characteristic of the animal alkaloids, but it is now known that many vegetable alkaloids give the same reaction, and a few of the animal alkaloids (especially those containing oxygen) do not give it. As yet there is no known class reaction by which the animal basis can be separated from those of vegetable origin.

THE URINE AS A TOXIN.

It has long been generally believed that normal urine is an auto-intoxicant. The well-known fact that suppression of the urine is invariably followed by certain uniform toxic symptoms ending in death seemed to leave no further proof of the truth of this belief necessary. It was not, however, until a comparatively recent period (1881) that Feltz and Ritter first demonstrated the actual toxicity of normal urine by injecting it into the blood of animals, thereby invariably invoking symptoms which were followed by death of the animals when the dose approached a certain relative amount. These experiments were soon after repeated and confirmed by Bocchi, Schiffer, and others. Two or three years later Dupard, Lépine, and Guérin established the special toxicity of certain pathological urines which has since been confirmed by numerous observers.

Following the researches of Feltz and Ritter, Bouchard commenced the investigation of the toxicity of normal urine, and very recently Lenoir gives a complete review of this subject, as does Charrin. The method of investigation pursued by Bouchard[1] consisted of intra-venous injections of urine in animals (chiefly rabbits), and the results would seem to have established the following conclusions:—

1. That the toxic power of normal urine as a whole is such that an average of 45 cubic centimetres of urine kills 1 kilogramme of living animal; and, therefore, the urine of two days and four hours contains sufficient toxic matters to kill a man of 60 kilogrammes weight.

2. The toxic symptoms induced by intra-venous injections of urine are as follow: (*a*) Myosis; contraction of the pupils beginning with the injection of 10 cubic centimetres to 15 cubic centimetres of urine per kilogramme; the pupils contracting to pinhole size, and thus remain until after death, after which they sometimes dilate. (*b*) The respirations become hastened and of diminished range. (*c*) Somnolence and coma follow. (*d*) Diuresis becomes marked, micturition occurring every two or three minutes. (*e*) Marked lowering of temperature succeeds. (*f*) Diminished palpebral and corneal reflexes are present. (*g*) Death succeeds in coma or convulsions. (*h*) The heart continues to beat for some time after death.

3. The toxicity of the urine varies with certain circumstances, viz.: (*a*) The urine is twice more toxic during the day than during the night. (*b*) The night urine is strongly convulsive and but feebly narcotic, while the day urine is the reverse,—strongly narcotic, but feebly convulsive. (*c*) Active muscular exertion in the open air diminishes the toxic power of the urine one-third, and this diminution of toxicity continues for from twenty-four to forty-eight hours after cessation of the exercise.

4. The toxicity of the urine is not due to urea, uric acid, or

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[1] Auto-Intoxication in Disease, Ch. Bouchard. Translated by T. Oliver. Published by The F. A. Davis Co., Philadelphia, 1894.

creatinin, since the injection of these substances into the blood in much larger proportional amounts than those in which they exist in normal urine proves non-toxic.

5. The toxicity of urine increases by permitting it to stand some time, as well as by increasing its temperature, even though fermentation be prevented. By this means a urine that ordinarily kills by coma becomes not only more toxic,—killing in smaller doses,—it also causes convulsions instead of coma.

6. The following facts are brought out regarding the isolation of the toxic elements of the urine: (*a*) If the urine be decolorized by charcoal it deprives it of about one-third (33 per cent.) of its toxic powers. (*b*) An aqueous extract of the urine (containing chiefly the mineral elements) causes contraction of the pupils, convulsions, and lowered temperature, but no coma, diuresis, or salivation. (*c*) An alcoholic extract of the urine produces somnolence, deep coma, and diuresis; but it does not cause contraction of the pupils or convulsions.

7. In acute uræmia the urine becomes non-toxic, and it may be injected into the blood in quantity equal to that of water (about 90 to 120 cubic centimetres per kilogramme) before it proves lethal, and then only mechanically, by interfering with the normal osmosis.

It will be seen, from these investigations, that normal urine owes its toxic properties not to any one, but to several constituents; and although Bouchard has not succeeded in completely isolating these, yet his results are suggestive in that direction. Briefly stated, his results are as follow: At least seven toxic agents are present in normal urine:—

1. A diuretic substance, which is fixed and of organic nature, non-removable by filtration through carbon, but is soluble in alcohol. This substance answers to all the features of urea, and is only toxic in enormous doses.

2. A narcotic substance, also fixed and of organic nature, non-removable by carbon, and soluble in alcohol. It is not urea, since it does not induce diuresis; but, on the other hand, it causes narcosis.

3. A sialogenous substance which produces salivation. It is only present in small amount in normal urine, and hence its

effects are unobservable in quantities of urine sufficient to kill from other contained toxic agents. This substance is stable, of organic nature, non-removable by carbon, and soluble in alcohol.

4. Two substances capable of causing convulsions: (*a*) One, fixed, stable, of organic nature, is both retained and destroyed by carbon, and is insoluble in alcohol. It is doubtless an alkaloid, and is present during the day in less amount than the narcotic substance, and also of less physiological activity than the latter. (*b*) A substance which causes myosis; it is fixed, organic, and removable by carbon. It is probably a coloring substance of normal urine.

5. A substance which reduces body-heat. It is fixed, of organic nature, and insoluble in alcohol. It may also be a urinary pigment.

6. Another convulsive substance of mineral nature, which is doubtless potassium.

Pathological Urine.—In pathological conditions the toxicity of the urine may become diminished, or it may become greatly increased. As a rule, in acute infectious diseases and fevers, if the kidneys remain unaltered, the urine becomes more powerfully toxic than in health. On the other hand, in pathological states of the kidneys themselves, the toxic powers of the urine become more or less diminished, according to the degree of functional incapacity of the kidneys. Thus, in acute nephritis or extensive chronic changes which greatly cripple the functional capacity of the kidneys, the urine may become almost non-toxic. As the condition of the kidneys improves the urine becomes more and more toxic, and this fact may be taken advantage of as a prognostic indication in treatment. For instance, if it require 80 cubic centimetres of urine to kill a rabbit of 1 kilogramme weight, it may be assumed that the capacity of the kidneys is crippled about one-half (50 per cent.). If in a week later 60 cubic centimetres of urine kill a rabbit of 1 kilogramme weight, it furnishes substantial evidence that the condition of the kidneys is much improved.

It has already been stated that the urine in acute uræmia is non-toxic. Under such circumstances the kidneys can no longer eliminate the usual toxic agents from the system, and the organism becomes poisoned—uræmic—and all the phenomena described as due to intra-venous injections of urine are evoked.

Our present knowledge of this subject warrants the statement that the healthy organism is only saved from *lethal* auto-intoxication by the liver and kidneys; the former destroys the larger proportion of the systemic toxins, and those not so destroyed are eliminated chiefly by the kidneys, if the latter be healthy.

In a large proportion of pathological urines (the kidneys remaining sound) the normal toxicity of the urine becomes increased, and, moreover, new toxic properties are developed, notably those with convulsive powers. Thus, in *tetanus* the urine is powerfully toxic, and if injected into the circulation it evokes most of the tetanic phenomena. M. Labbe injected the urine of a tetanic patient into the circulation of an animal, with the following results: After the sixth cubic centimetre (per kilogramme) mild tremors occurred; the pupils became punctiform at 10 cubic centimetres. From 12 cubic centimetres violent tonic spasms with convulsions occurred up to 34 cubic centimetres. At the latter point death occurred from opisthotonos.

The urine in *pneumonia* is strongly toxic, the symptoms being nearly as pronouncedly convulsive as in the case of tetanus. The urine in pneumonia proves *lethal* in from 19 cubic centimetres to 38 cubic centimetres per kilogramme. In *typhoid fever*, on the other hand, Bouchard has observed that the urine produces only the toxic symptoms of normal urine; death occurs at from 50 to 70 cubic centimetres per kilogramme with only slight myosis, coma being present, but not convulsions. In *leucocythæmia* the urine is highly toxic, causing convulsions and death at 15 to 20 cubic centimetres per kilogramme.

The urine possesses special and marked toxic powers in *cholera*. Thus, cyanosis is only produced by choleraic urine; muscular cramps follow, unlike the convulsions produced by other urines, since the spasms begin long after the beginning of the injections, and they continue long after the injections are discontinued. Cooling of the body is more pronounced than from injections of any other urine. Albuminuria appears at once and in marked degree, while with normal urine albuminuria is rare and only occurs late. Diarrhœa always follows injections of choleraic urine; the stools become pale, watery, and devoid of bile. The albuminuria increases until complete anuria occurs, in about thirty-six hours, and death soon after occurs with a rectal temperature of 33° or 34° C.

SECTION VI.

URINARY SEDIMENTS.

URINARY sediments are most conveniently classified, for purposes of study, into two divisions, viz., *chemical substances* and *anatomical substances.*

Chemical sediments, with but few exceptions, exist in the form of solution in normal urine, and their appearance as crystalline, amorphous, or other form of sediments may result from excessive formation or excessive excretion, or alterations in the urine affecting its solvent powers. The chief chemical deposits met with in the urine are uric acid, the urates, calcium oxalate, cystin, leucin, tyrosin, xanthin, and phosphates.

The *anatomical sediments* are in most cases foreign substances, and therefore do not exist in normal urine. They consist of such structures as pus-corpuscles, blood, renal casts, spermatozoa, fragments of growths, fungi, infusoria, etc. The anatomical elements found in the urine are more or less insoluble, and, therefore, when the urine stands they fall to the bottom as sediments.

Our methods of examining urinary sediments are both chemical and microscopical. Thus, the chemical deposits may often be recognized by their characteristic reactions; or the microscope may be employed to determine the characteristic form of the deposit when crystalline, which is often of itself diagnostic. In determining the character of the anatomical deposits the microscope constitutes the chief resource, although, in some cases, chemistry materially aids the investigation.

SEDIMENTATION OF URINE.

The older method of obtaining urinary sediments for investigation consisted in letting the urine stand in conical vessels for twenty-four hours or so, when the sediment would usually be found collected in the bottom of the vessel. Much difficulty was formerly encountered by this method in securing sediments for examination which remained unchanged, since the length of time necessary to secure the deposit almost necessarily involved alterations in the urine at ordinary temperatures. Of late years this has been in a measure overcome by the addition of preservative agents to the urine, such as chloral hydrate, salicylic acid, resorcin, etc. These, however, all interfere with the chemical examination of the urine, more especially in making examinations for sugar and urea. But the most serious objection to the old method was the necessity of waiting for several hours before a satisfactory microscopical examination of the urine could be made.

More recent experience has demonstrated the immense advantages of the centrifugal method of obtaining urinary sediments for purposes of microscopical examination. The principle of this method depends upon the fact that when the urine is placed in tubes and revolved upon horizontal rotating arms at a high speed, a centrifugal force is exerted upon all solid particles in the urine hundreds of times greater than gravity; and, consequently, the urinary sediment is deposited in the bottom of the tubes almost immediately, irrespective of the specific gravity of the urine or the character of the sediment. Some of the advantages of this method are as follow:—

1. Centrifugal sedimentation of the urine permits of an immediate microscopical examination, instead of waiting for from twelve to twenty-four hours by the old method of gravity.

2. The centrifugal method secures more complete and concentrated sedimentation, and therefore it is better suited for purposes of microscopical diagnosis.

3. Microscopical examination may be made of freshly-voided urine before casts or morphological elements have had time to undergo maceration or solution in the urine, and before bacterial fermentation occurs, which always greatly obscures the microscopical field.

4. It affords the only positive means of distinguishing between normal and abnormal *crystalline* sediments in the urine, because by the centrifugal method only can the urine be examined by the microscope as soon as voided, and, therefore, before the crystals form which are deposited in all normal urines after standing.

5. By the old method of gravity it sometimes happened, with urines of high specific gravity, that the lighter casts (such as those of the narrow, hyaline order) failed to settle, and thus eluded detection. The centrifuge precipitates all casts without delay, irrespective of the above-named conditions.

6. In consequence of the greater concentration of the urinary sediment by the centrifuge, bacterial search is rendered more simple and successful; micro-organisms, such as *tubercle bacilli*, being found with greater ease and certainty.

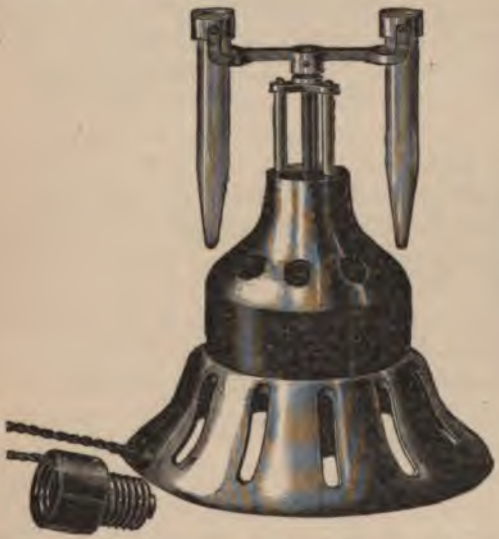

FIG. 12.—THE AUTHOR'S ELECTRIC CENTRIFUGE. (One-fourth actual size.)

It will therefore be readily seen that the centrifuge is destined to rapidly supersede the old method of gravity for all purposes of urinary sedimentation.

Various forms of the centrifuge are manufactured for urinary purposes, and may be obtained of the leading instrument dealers. At present, the best hand-power centrifuge for urinary purposes is made by R. Jung, of Heidelberg. For practical work, the centrifuge should be capable of a speed of at least 1000 revolutions per minute. The accompanying cut (Fig. 12) shows the electric centrifuge especially designed by the author for urinary work.

By means of this apparatus, renal casts, epithelium, pus, blood, bacteria, crystals, etc., and, in short, all urinary sediments, —organic and inorganic,—can be sedimented at once, thus affording an immediate microscopical examination where formerly it required hours or even days to obtain the same results by the old method of gravity.[1]

The author's electric centrifuge is capable of a maximum speed, *without tubes*, of over 6000 revolutions per minute, by multiple resisters on the 110-volt current; with *small*, *light* sediment tubes, it is capable of a speed of from 2500 to 3500 revolutions per minute; with *large tubes* (carrying one ounce of urine) it attains a speed of 1500 to 2000 revolutions per minute. The precipitating centrifugal force exerted by this centrifuge is 2000 times greater than gravity, and, therefore, a sediment requiring twenty-four hours to precipitate by gravity may be obtained by this centrifuge in less time than two minutes. In throwing down sediments for purely microscopical purposes, the best grade of speed, as a rule, is 1200 to 1500 revolutions, although higher speed may be employed if desired. In other words, the author finds for this purpose that *medium speed and proportionate increase of time give the best results.* Bacterial search forms an exception to this rule, high rates of speed in such cases being preferable.

The author's electric centrifuge, by reason of its special design and construction, the field and armature of the motor being specially wound, can be operated by currents of 110 volts direct (with resisters) or 52 volts alternating. It therefore possesses the unusual advantages of operating by either direct or alternating currents without overheating. It may hence be operated by the currents of any of the existing systems of electro-incandescent lighting. It can also be operated by either the ordinary galvanic or storage currents. This centrifuge is armed with aluminium shields for the glass sediment tubes, which prevent all danger from breakage of the latter at the highest attainable speed. Attachment-plugs, resisters, aluminium shields, sediment and percentage tubes, and all accessories are furnished by the manufacturers.[1] The cost of the whole apparatus, with the accessories necessary for sedimentation for microscopical purposes, as well as for percentage centrifugal analysis of urine, is only a trifle more than that of the hand-power centrifuge made by R. Jung, of Heidelberg.

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[1] By means of percentage tubes and special methods devised by the author (see Section II, page 64), quantitative percentage determinations may be made by this centrifuge of chlorides, phosphates, sulphates, albumin, pus, etc., and this method will be extended to include as many of the constituents of the urine, normal and abnormal, as will be found practicable and advantageous.

It may be stated, in conclusion, that the immense convenience and saving of time effected by centrifugal methods, as applied to uranalysis, can only be fully appreciated by those who have employed them. By the aid of the electric centrifuge, complete qualitative and quantitative examinations of the urine, including microscopical search, are daily made in the author's laboratory within twenty minutes.

From a somewhat extensive experience in the use of the centrifuge in urinary work, the author finds that the old form of bulb-tipped sediment tube is very unsatisfactory where the amount of sediment is small: the sudden stoppage of the centrifuge creates currents in the bulb that often dislodges the sediment and causes it to rise in the tubes. The new form of sediment tubes (Fig. 13), devised by the author for his electric

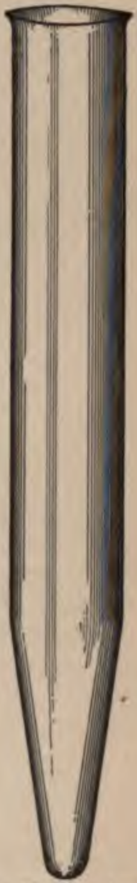

FIG. 13.—THE AUTHOR'S SEDIMENT TUBES FOR CENTRIFUGAL SEDIMENTATION. (Full size.)

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[1] The author's centrifuge is manufactured and supplied by the Wood Electric Manufacturing Co., Nos. 18 and 30 West Randolph Street, Chicago.

centrifuge, completely obviates this difficulty; in fact, the urine may even be decanted, and the sediment will remain in the bottom of the tubes. These conical-tipped tubes also lessen the degree of atmospheric pressure where the resistance is greatest—at the ends of the tubes; and both the bulk and weight of the tubes being carried nearer the centre, considerable increase of speed is obtained by the centrifuge without increase of motor power.

In searching for urinary deposits it is of prime importance to deal with a freshly-voided sample of urine. As already noted, the urine is a very unstable fluid, and at ordinary temperatures chemical alterations very soon occur, which may dissolve or so alter either the chemical or anatomical deposits as to render them altogether difficult or even impossible of rocognition. Moreover, in consequence of these changes, a series of deposits occur in all normal urines, upon long standing, with which it is well to become familiar.

Strictly normal urine of *acid* reaction, when freshly voided, is transparent and free from sediment. After standing some time, there forms, in the lower third of the volume of urine, the "*nebecula*,"—a slight haze, consisting of mucus, carrying with it a few mucous corpuscles and flat epithelia, thrown off chiefly from the bladder-walls. The *nebecula* may be most readily seen by holding the urine up to a good light with a dark but narrow background intervening; or it may be quickly precipitated by the centrifuge, when it will be found to consist of mucus entangling epithelial cells and a few mucous corpuscles. Upon longer standing, strictly-normal urine of *acid* reaction gradually deposits (*first*) a reddish-yellow or clay-colored sediment of amorphous urates of potassium, sodium, and ammonium, and occasionally of calcium and magnesium, which are readily soluble by heat; (*second*) and, some time later, the above-described sediment is more or less replaced by beautiful, brick-red or dark-brown, sharply-outlined crystals of uric acid; (*third*) at the same time, or later still, there forms among the uric-acid crystals, or are replaced by them, octahedral or envelope-shaped, highly-refracting crystals of calcium oxalate; (*fourth*) and at a still later, though variable, period, strictly normal urine deposits a sediment composed of the phosphates of the alkaline earths,—granular, amorphous calcium phosphate and triangular, prismatic crystals of triple phosphate of ammonium and magnesium, often interspersed by dark spherules of ammonium urate with attached, sharp spicula.

Again, in strictly-normal urine of *alkaline* reaction, such as frequently occurs in the morning, or three or four hours after a meal, there frequently deposits a whitish, flocculent sediment, of considerable bulk, consisting of the granular, earthy phosphates. These may be made to quickly disappear by destroying the alkalinity of the urine by means of a few drops of any strong acid.

The explanation of these changes has already been made in Section I, page 5. The importance of procuring fresh urine for sedimentary investigation will therefore be seen at once, since nearly every inorganic and many organic substances in normal urine are liable to be deposited upon long standing, when such deposits are neither evidences of excess of the deposited substances nor of existing pathological conditions.

When insoluble substances in the urine remain in suspension, they produce more or less turbidity; but when they subside to the bottom, they constitute a deposit. Precipitation occurs with varying degrees of facility in different urines, both by standing and by centrifugation, but less so by the latter, depending in part upon the consistence and density of the urine, and in part upon the nature of the sediment. Thus, precipitation is more rapid in watery urines—as in hysteria and diabetes insipidus—than in thick, albuminous, or saccharine urines. Again, the heavier crystalline deposits, such as uric acid, the urates and oxalates, precipitate rapidly; while such substances as epithelium, pus-corpuscles, and hyaline casts deposit very slowly. In tuberculous conditions of the urinary organs much of the insoluble products of ulceration remain more or less permanently suspended in the urine upon standing,—only the more solid and heavier products being precipitated,—and this is considered, in a measure, diagnostic of tuberculous urine.

CHEMICAL SEDIMENTS.

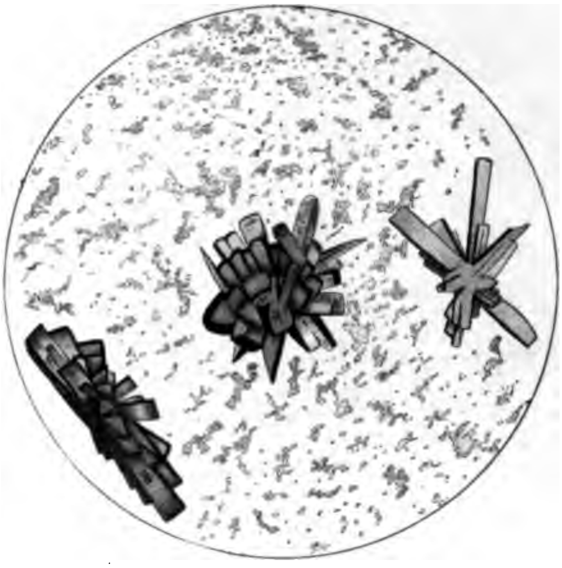
LITHURIA.

Uric-acid crystals occur as a sediment rarely, if ever, in other than sharply-acid urine. They differ from all other urinary deposits in possessing a deep-yellow or orange-red color; they may at times be pale yellow, but are never colorless. The crystalline nature of this deposit may usually be detected readily by the naked eye. The essential or primary form of the uric-acid crystal is that of rhombic prism, and the great variety in which it is found all constitute combinations or modifications of this form. Thus, the angles may be nearly equal, forming quadrangular plates, or sometimes nearly cubes may be seen. Again, they may be seen with rounded ends, forming ovoids or circles. Elongated crystals are sometimes observed, and these frequently join at one end, forming stars. The beauty and variety of these star-shaped clusters are very marked. (See Plate III.) Sometimes fan-shaped forms are produced by elongation of the crystals in one direction only, instead of the star form. The rough and pointed forms of uric-acid crystals are claimed by Ultzmann to be of diagnostic significance, being "almost always an accompaniment of renal calculi." For properties and tests of uric acid, see Section II, pages 30 to 36.

Uric acid possesses a strong tendency to crystallize upon contact with any solid substance, organic or inorganic. This may be observed by its behavior in a vessel upon standing, when it will often be noted that the crystals cling to the sides of the glass or to threads or specks suspended in the urine. This tendency renders it more liable than any other crystalline deposit to form around some nucleus in the urinary channels, and ultimately form gravel. This is one of the reasons why nearly 70 per cent. of the stones found in the bladder are of the uric-acid variety.

The deposit of uric-acid crystals can only be regarded as of pathological import when the deposit occurs shortly after the urine is voided,—say, within four to six hours. It has already been shown that perfectly healthy urine usually deposits uric-acid crystals after standing ten or more hours. But, on the

PLATE III.



Uric Acid Crystals with Amorphous Urates.
(After Peyer.)

other hand, if uric acid be precipitated from the urine shortly after it cools, it very justly forms the foundation for fear that the same may occur before it be voided, and thus give rise to the formation of calculi and gravel, with the long train of painful symptoms entailed by such conditions. Before speaking of the pathological conditions which usually attend deposits of uric acid, it may be well to allude to the conditions of the urine which favor such deposits.

Sir William Roberts, who has carefully investigated this subject recently,[1] makes the following interesting observations:—

"The presence of uric acid in human urine is somewhat anomalous, as it is not needed as a vehicle for the elimination of nitrogen. Its place is taken by urea, which, by its easy solubility, is better adapted to the liquid urine of animals. Perhaps uric acid is a vestigial remnant in mammalian descent. But, although physiologically insignificant, uric acid is pathologically the most prominent component of the urine, chiefly because of its tendency to form concretions.

"All acid urines tend inevitably to deposit their uric acid sooner or later. The time of onset of precipitation varies from a few hours to five or six days, or even longer. The inference from this is that pathological gravel is due to an exaggeration of conditions which exist in a less pronounced degree in health. To get at an explanation of this spontaneous precipitation it is necessary to examine the states of combination of uric acid in the urine.

"Uric acid ($C_5H_4N_4O_3 = H_2U$) is a bibasic acid, and forms two regular orders of salts, namely, *neutral* or *normal urates* ($M_2\bar{U}$) and *acid urates* or *biurates* $(MH\bar{U})^2$. But, in addition to these, it forms a series of hyperacid combinations, first discovered by Bence Jones, and termed by him *quadrurates* ($MH\bar{U}.H_2\bar{U}$). The neutral urates are never found in the animal body, and are only known as laboratory products. The biurates are only encountered pathologically as gouty concretions. The quadrurates, on the other hand, are especially the salts of uric acid. They constitute the exclusive combination in which uric acid exists in solution in normal urine, and they become visible sometimes as the amorphous urate sediment. The urinary excretion of birds and reptiles is composed exclusively of quadrurates. The special and characteristic reaction of quadrurates is that they are immediately decomposed by water into free uric acid and biurates. They exist in acid urine in the presence of water and of superphosphates. These conditions necessarily involve the ultimate liberation and precipitation of uric acid. The first step is the breaking up of the quadrurate by the water of the urine into free uric acid and biurate, according to the following equation:—

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[1] Proceedings of the Medico-Chirurgical Society, 1890, p. 85.

$$\underset{\text{Quadrurate.}}{(MH\bar{U}.H_2\bar{U})} + H_2O = \underset{\text{Free uric acid.}}{(H_2\bar{U})} + \underset{\text{Biurate.}}{(MH\bar{U})}.$$

"This explains the liberation of half the uric acid. But the biurate thus formed is forthwith changed in the presence of superphosphates into quadrurates. Thus:—

$$\underset{\text{Biurate.}}{2(MH\bar{U})} + \underset{\text{Superphosphate.}}{(MH_2PO_4)} = \underset{\text{Quadrurate.}}{(MH\bar{U}.H_2\bar{U})} + \underset{\text{Dimetallic phosphate.}}{(M_2HPO_4)}$$

By these alternating reactions all the uric acid is at length set free.[1]

"Seeing that uric acid exists in acid urine (that is, for some sixteen hours out of the twenty-four), amid conditions which, if the quadrurates stood alone and uncontrolled, would lead to its immediate precipitation, and yet that in the normal course no such early precipitation occurs, it is obvious that the urine must contain certain ingredients which inhibit or greatly retard its water from breaking up the quadrurates. These inhibitory ingredients consist chiefly of (1) the mineral salts and (2) the pigments of the urine. The conditions of the urine which tend to accelerate the precipitation of uric acid, as in the formation of concretions and deposits, are (1) high acidity, (2) poverty in mineral salts, (3) low pigmentation, and (4) high percentage of uric acid. The converse conditions tend to retard precipitation. On the interaction of these factors the occurrence or nonoccurrence of uric-acid precipitation appears to depend, and probably the most important of these factors is the grade of acidity."

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[1] In these formulæ the symbol M represents a monad metal, and the symbol $\bar{U}$ the radicle $C_5H_2N_4O_3$.

Clinical Significance.—Uric-acid sediments are perhaps most often encountered in acute fevers and inflammations attended by pronounced elevation of temperature. In such cases there is diminution of the aqueous elements of the urine, entailing increased acidity. As a consequence of increased tissue metabolism, there is also absolute increase of uric acid, as of most other urinary solids. In the so-called *uric-acid diathesis* there is often an habitual and pronounced deposit of uric-acid crystals in the urine. The causes of this state are partly defective physiological action of the liver, and partly errors in diet, coupled with sedentary habits of life; and it is often accompanied by headache, emaciation, and hypochondriasis. Since this condition is induced by faulty habits of living which entail overwork of the liver, with defective supply of oxygen, it in nowise merits the name of "*diathesis.*"

In the early stages of interstitial nephritis, uric-acid deposits are often to be observed; indeed, the urine frequently throws down this deposit habitually for some time before the interstitial defect is made known by pronounced symptoms. This is due to two causes: (*a*) the polyuria of the early stages of the disease lessens the relative amount of coloring matters in the urine, and it will be remembered that the pigments tend to hold the uric acid in solution; (*b*) both interstitial nephritis and uric-acid deposits are often the outgrowth of the same habits of living, viz., the overindulgence in animal foods. The author has repeatedly observed that people who possess generous appetites, and indulge in the use of animal foods two and three times daily, are exceedingly apt to have uric-acid deposits in their urine at middle age, and somewhat later to develop interstitial nephritis. Uric-acid deposits are frequent in cases of children convalescing from scarlatina, with or without accompanying nephritis, and concretions or gravel are very prone to arise under such circumstances.

URATES.

The acid urates of *sodium*, *potassium*, *ammonium*, and, more rarely, of *calcium* are met with as sediments in the urine.

The acid urate of sodium occurs chiefly as minute, irregular, amorphous granules, although sometimes, also, in crystalline form,—star-shaped, needle-like clusters, often of fan-shape arrangement. This deposit is more or less deeply stained brown or pink, according to the degree of pigmentation of the urine, since it possesses a great affinity for the above-named pigments.

The sodium-urate deposit occurs in acid urine, and forms a large bulk of the "brick-dust," or mixed urate, deposit found in the bottom of the vessel after the urine has cooled. Acid sodium urate is extremely insoluble, requiring 1150 parts of cold or 124 parts of boiling water to effect its solution.

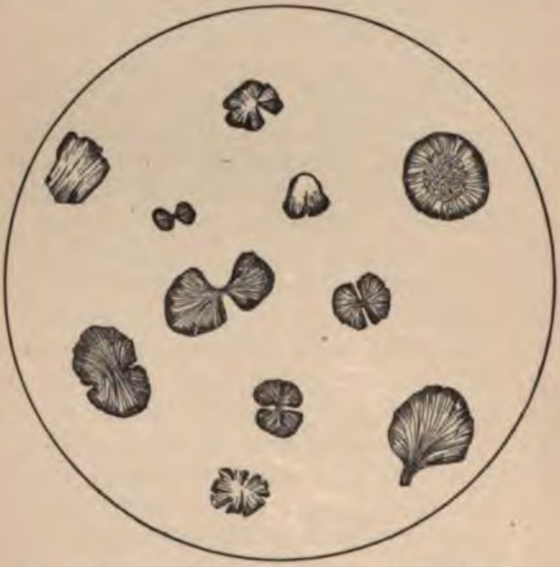
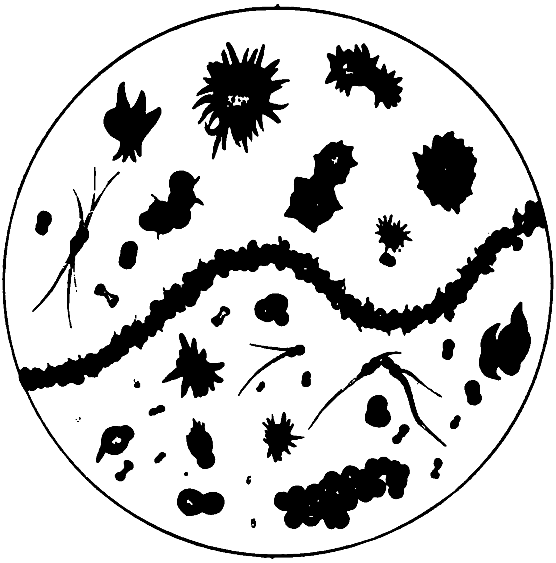


FIG. 14.—SODIUM-URATE CRYSTALS. (After Peyer.)

Acid potassium urate occurs only in amorphous form as a deposit, and, like sodium urate, forms a part of the mixed urate deposit met with in acid urines. It is much more soluble than the sodium urate.

Acid calcium urate occurs as a urinary deposit but rarely, and in minute quantities. It consists of a white or grayish

PLATE IV.



Ammonium Urate, showing Spherules and Thorn-apple-shaped Crystals. (After Peyer.)

amorphous powder, highly insoluble, and on fusion leaves a white residue, consisting of calcium carbonate. The acid calcium urate, like the potassium and sodium urate deposits, occurs only in acid urine.

Ammonium urate occurs as a crystalline deposit, consisting of dark-brown, spherical masses studded with fine, sharp-pointed spicula,—"*thorn-apple crystals.*" The spicula may be long, sometimes curved, branched, or bent, forming various shapes. (See Plate IV.) The smaller crystals often closely resemble those of sodium urate, and by some they are claimed to be identical.

This sediment most frequently occurs in alkaline urine, associated with amorphous calcium phosphate and triple phosphate crystals. The ammonium-urate deposit is, in fact, the only urate sediment found in alkaline urine.

The *mixed urate deposit* consists of a reddish, granular-looking sediment, with color always deeper than the urine from which it precipitates. It may vary all the way from a faint pinkish haze to a brick-red color. (See Plate III.) Most frequently it sinks quickly to the bottom of the quiescent vessel, but part of it may long remain suspended, imparting to the urine an opalescent turbidity; at the same time a pellicle may form on the surface or cling to the sides of the vessel, notably at the surface-line of the urine. By gently heating the urine the mixed urate sediment promptly dissolves, and this forms a ready method of its recognition, as no other urinary deposit behaves similarly. The mixed urate deposit gives the murexide reaction similar to uric acid. It is dissolved by solutions of the caustic alkalies; with mineral acids it is decomposed, with resulting precipitation of uric-acid crystals.

It is an interesting fact that urines of high density are most prone to throw down deposits of mixed urates, while those of lower density are more apt to throw out of solution uric acid. Thus, with urines of specific gravity at 1026 to 1030, when they cool, the excess of urates come down because of their limited degree of solubility; while in urines of specific gravity below 1020, the diminished pigmentation often permits the uric acid to fall out of solution and form a deposit.

Clinical Significance.—The mixed urate deposit, like that of uric acid, is most frequently encountered in febrile states; even a slight elevation of temperature is often sufficient to cause their deposit. A more constant deposit of mixed urates may be noted in diseases of the viscera, which entail progressive emaciation, notably in the liver and in the so-called wasting diseases. Functional disorders of the stomach are frequently associated with amorphous urate deposits, due, in all probability, to incomplete transformation of proteid foods. In gout the urates are usually deposited during the attack, but disappear upon the approach of convalescence.

OXALURIA.

Oxalate of lime is met with as a urinary sediment either in acid or alkaline urine, but most often in the former. If it occur in acid urine it is often associated with uric-acid deposits, but when occurring in alkaline urine its most frequent associated deposit is the triple phosphate.

The calcium-oxalate deposit occurs in crystalline form, consisting chiefly of two varieties of crystals, (*a*) and most frequent are the octahedral crystals, very beautiful and highly refracting. They are made up of four-sided pyramids, situated base to base, as seen in their long diameters. When viewed from the side they appear as squares crossed obliquely by two sharp lines, forming the characteristic "*envelope-shaped*" crystals. When small, the lines crossing in the centre form a bright spot, highly refractive of light,—star-like. (*b*) The second form of calcium-oxalate deposit is the so-called "*dumb-bell*" crystals. Their true form is that of ovoid or circular disc, with round margins and depressed at the centre on either side. Their variable appearance depends upon their different positions when viewed, as may be seen by causing the crystals to roll over under the cover-glass.

Calcium oxalate is insoluble in alcohol, ether, water, alkalies, and acetic acid, but readily soluble in hydrochloric or other mineral acids,—characteristics which serve to identify this salt; but in practice the microscopical appearance is the most conclusive, since the crystals are so characteristic in form that they are readily distinguishable from all other crystalline deposits; the deposits of triple phosphate and uric acid are the only ones which have the least resemblance thereto.

With regard to the triple-phosphate crystals, it is only the smaller, imperfect, and short prisms that are ever confounded with calcium-oxalate crystals. In such cases the body of the crystals, instead of forming a parallelogram, is shortened so that it becomes a square, and the prism then gives somewhat the appearance of the envelope-shaped calcium-oxalate crystal. The calcium-oxalate crystals, however, are always smaller and more highly refracting. Should any doubt remain, after careful ocular examination, they may be readily distinguished by their behavior with acetic acid, which promptly dissolves the triple-phosphate crystals, while the calcium oxalate is unaffected thereby.

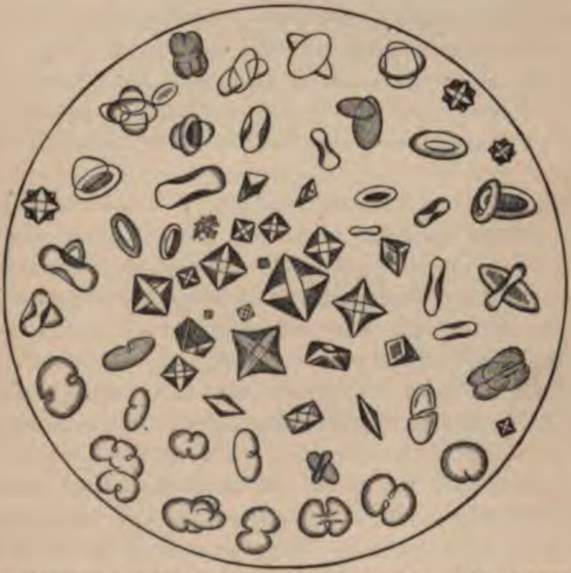


FIG. 15.—VARIOUS FORMS OF CALCIUM-OXALATE CRYSTALS. (After Peyer.)

The "dumb-bell" form of uric acid may usually be distinguished from the calcium-oxalate crystals of similar form by the brown color of the former, as well as by their solubility in alkalies.

Clinical Significance.—The occurrence of calcium oxalate as a urinary deposit is brought about by the strong affinity which oxalic acid possesses for calcium. Oxalic acid occurs under physiological conditions in very small amounts in urine,—about 0.02 gramme in twenty-four hours. According to generally received opinion, it exists in the form of calcium oxalate, which is kept in solution by the acid phosphates of the urine. The quality of food taken often materially influences the degree of physiological oxaluria. Thus, vegetables containing much oxalic-acid combinations,—as cabbage, spinach, asparagus, sorrel, apples, grapes, tomatoes, turnips, and sugar,—when taken in excess, may cause excretion of calcium oxalate in considerable amount. Calcium oxalate is also excreted in excess upon an exclusive or excessive diet of flesh and fat, indicating its formation from proteids.

The question of so-called "*oxalic-acid diathesis*" possesses much practical interest. As early as 1842, Bird described a series of nervous and dyspeptic symptoms, which he alleged were associated with deposits of calcium oxalate in the urine. Later on, Bigbie still more minutely described the symptoms of the so-called "*oxalic-acid diathesis*," of which the following is a brief summary: "These patients are mostly males in the prime of life, ordinarily of sanguineous or melancholy temperament, of sedentary habits, and accustomed to overindulgence in the luxuries of the table. Indigestion in its varied forms is a prominent feature. These patients are often capricious, sensitive, irritable, or dull, despondent, and melancholic. The tongue is coated and the skin is dry. In inveterate cases a dirty, dingy countenance, increasing emaciation, falling out of the hair, tendency to boils, carbuncles, psoriasis, and other cutaneous disorders are frequently observable. Accompanying these are often deep pains in the back and loins, hæmorrhages from the intestines and bladder, incontinence of urine, impotence and irritation of the bladder."

Attractive though the theory be of the so-called "*oxalic-acid diathesis*," in the light of more recent and wider observation the name "*diathesis*" seems in nowise merited by any of the states associated with deposits of calcium oxalate in the urine.

It is true that oxalic acid, when taken internally in any considerable amount, exerts a poisonous action upon the organism, not only locally on the intestines, but also generally on the heart and nervous system; and this gave rise, no doubt, to the supposition that a large formation of oxalic acid or its retention in the system might produce toxic, and even dangerous, symptoms. Distinct proof, however, is yet lacking to show that the symptoms of the so-called "*oxalic-acid diathesis*" are due to an accumulation of oxalic acid in the blood. Indeed, nearly all the evidence tends in the opposite direction. In the first place, large deposits of calcium oxalate, and even the formation of oxalic calculus, is repeatedly observable in people who are otherwise in the enjoyment of the most typical good health. In the second place, the group of symptoms described as characteristic of the oxalic-acid diathesis, as Roberts has observed, "is one common to the clinician minus the deposits of calcium oxalate." Lastly, the states of the system associated with deposits of calcium oxalate are altogether too varied to admit of so narrow a classification as that of a special diathesis. It seems most reasonable to conclude that oxaluria is dependent upon a variety of conditions of the system, many of which are associated with little or no departure whatever from ordinary health.

The conclusions of Beneke, who has thoroughly investigated this subject, are as follow:—

1. Oxaluria accompanies the lighter or severe forms of illness; has its proximate cause in an impeded metamorphosis,—*i.e.*, in an insufficient activity of that stage of oxidation which changes oxalic acid into carbonic acid.

2. Oxalic acid has its chief source in the azotized constituents of the blood and food; hence, everything which retards the metamorphosis of these constituents gives rise to oxaluria.

3. Such retardation of the metamorphosis of azotized elements of the blood may be determined by the following causes: (*a*) excessive use of azotized articles of food; (*b*) excessive use of saccharine and starchy articles of food; (*c*) insufficiency of the red blood-corpuscles, entailing diminished oxidation; (*d*) insufficient access to pure fresh air; (*e*) organic lesions which in any way impede respiration and circulation; (*f*) conditions of

the nervous system entailing depression, whether arising primarily from mental derangement or from pathological states of the blood.

4. Excess of alkaline bases in the blood.

Phosphaturia.

It has already been shown in Section II that phosphorus exists in normal urine in combination with the alkalies and the earths,—the alkaline and earthy phosphates. It is only, however, the latter salts that are met with as urinary deposits. The earthy phosphates consist of (*a*) triple phosphate or ammonio-magnesium phosphate, and (*b*) calcium phosphate or phosphate of lime.

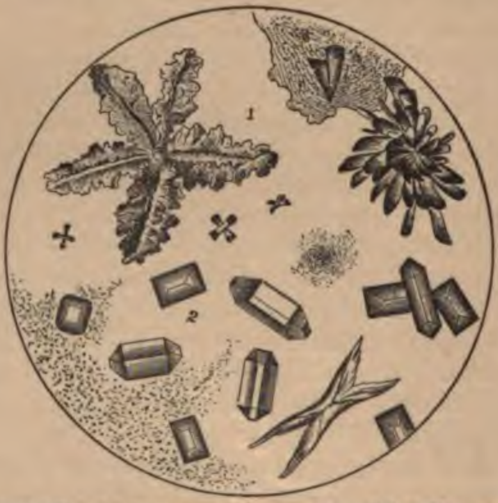


Fig. 16.—Triple-Phosphate Crystals. (After Ultzmann.)
1. Rosette or star-shaped crystals. 2. Coffin-shaped crystals.

Ammonio-magnesium phosphate ($MgNH_4PO_4 6H_2O$), or triple phosphate, is essentially a crystalline deposit, occurring in two forms. The first—most frequent and typical—form is that of a triangular prism with beveled ends, very distinctive and often termed "*coffin-shaped*" crystals. Many modifications of this typical form are met with. Thus, the crystals may be shortened to the form of squares, instead of being oblong, or one or more corners may be absent.

The second and less frequent form in which triple phosphate appears as a urinary sediment is that of star-shaped, feathery crystals, the points appearing not unlike fern-leaves. These are often but rudiments of the prismatic form of triple-phosphate crystals, into which latter they often become gradually transformed, and therefore between these two forms numerous intermediate ones are to be observed (Fig. 16).

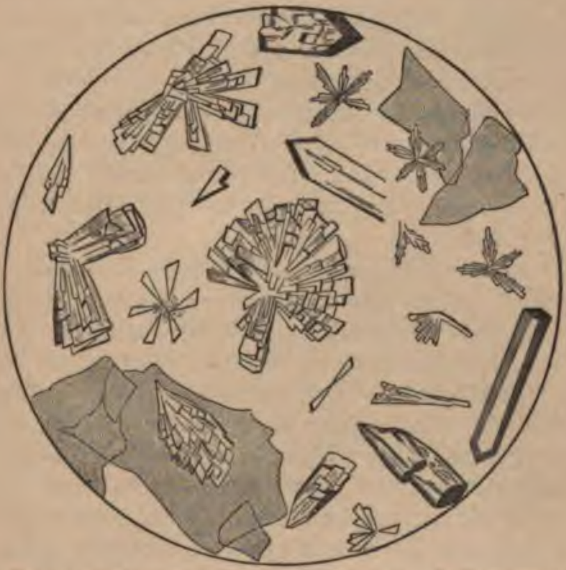


FIG. 17.—CALCIUM-PHOSPHATE CRYSTALS. (After Peyer.)

Calcium phosphate is met with as a urinary sediment in two forms,—(*a*) *amorphous*, (*b*) *crystalline*. The amorphous form of calcium phosphate is a whitish, flocculent deposit, often mistaken by the naked eye for pus or granular organic matter, and when precipitated from the urine by heat it is sometimes mistaken for albumin. Under the microscope this sediment appears in the form of minute, pale granules, arranged in irregular patches.

The crystalline form of calcium phosphate is a comparatively rare deposit, occurring less frequently than any other form of phosphatic deposit. Its essential or elementary form is that of crystalline rods, sometimes lying unarranged, but more often grouped in stellar or rosette form, while often they may be observed grouped in club or wedge form, but always marked by lines of crystallization (Fig. 17). The earthy phosphates are essentially a product of alkaline urine, and, with the exception of the crystalline form, they are never met with in acid urine. The above-named exception only occurs with feebly-acid urine tending to ammoniacal change.

The following are the chief conditions of the urine which lead to phosphatic sediments :—

(*a*) If the urine be alkaline from fixed alkali.

(*b*) If the earthy phosphates be in excess (the urine being alkaline or neutral).

(*c*) If the urine be alkaline from volatile alkali, the result of decomposition of urea into ammonium carbonate in the urinary passages, the ammonium uniting with the magnesium phosphate to form the triple phosphate of ammonium and magnesium.

Clinical Significance.—In those cases in which the phosphatic deposit occurs in alkaline urine from *fixed* alkali, the deposit is chiefly precipitated calcium phosphate, though often mixed with triple-phosphate crystals. The urine in these cases is usually of high specific gravity, alkaline in reaction *when voided*, more or less cloudy, and effervesces upon the addition of acid, after which the urine immediately clears. The clinical symptoms corresponding to the above are often those of general debility, with feeble respiration—favoring the accumulation of carbonic acid in the system. Thus, in convalescence from exhausting acute diseases, deposits of calcium phosphate are frequently to be noted. Flatulent dyspepsia is a frequent cause of alkaline urine from fixed alkali and the deposit of calcium phosphate.

As Ralfe has pointed out, the acids formed by fermentative changes being of the fatty acid series, upon entering the blood they are oxidized into carbonic acid, and, uniting with the bases of the alkaline oxides from carbonates of these bodies, increase the alkalescence of the blood and in consequence diminish the acidity of the urine or even render it alkaline, which permits the phosphates to fall out of solution. This is most frequently noted in debilitated persons with flatulence of the small intestine. It is associated with such features as loss of weight, irregular bowels, sallowness of complexion, despondency, and frequent micturition.

In those cases in which the deposit of calcium phosphate is the result of excessive elimination, very often marked systemic disturbances are associated therewith. The urine is usually alkaline, copious in volume, and the deposit is of dense whitish form. If persistent, the symptoms are usually those of nervous irritability, dyspepsia, emaciation, and backache. Sometimes symptoms akin to diabetes are observable in inveterate cases, and the condition has been called "*phosphatic diabetes.*" Indeed, it is claimed that this condition not infrequently ends in diabetes insipidus.

The deposit of the crystalline form of calcium phosphate in quantity is, in the experience of Roberts, often "an accompaniment of some grave disorder," such as cancer of the pylorus, phthisis, and exhaustion from obstinate chronic rheumatism.

In cases of phosphatic deposits in the urine resulting from the presence of volatile alkali, the sediment, as before stated, is that of triple phosphate of ammonium and magnesium. It has already been shown that ammoniacal fermentation always occurs in healthy urine upon standing sufficiently long, and then the triple phosphates are precipitated. But in the class of cases under present consideration the urine is alkaline *when voided* and precipitation of triple phosphates takes place immediately. In these cases ammoniacal decomposition of the urine occurs in the urinary passages. In addition, therefore, to the triple-phosphate deposits in such cases, the urine also contains pus and more or less mucus.

The clinical symptoms attending this state of the urine are most often those of septic inflammations of the urinary passages, such as pyelitis and cystitis. The most frequent class of causes of this condition of urine are the obstructive diseases of the lower urinary conducting channels. Whatever cause operates to retain the urine in the bladder sooner or later gives rise to cystitis and the deposit of triple-phosphate crystals. Thus, in enlarged prostate, atony and paralysis of the bladder, paraplegia, and diseases of the lower spinal cord, the urine nearly always precipitates the triple phosphates. This condition of urine nearly always precedes so-called "*surgical kidney*," and those septic conditions so dangerous to life which result from the use of instruments in the lower urinary channels. Therefore, when the urine is found to contain deposits of triple phosphate with pus, and is alkaline when voided, it constitutes a signal for the exercise of the greatest possible caution on the part of the surgeon in passing instruments into the urethra and bladder for the *first time*, more especially in the cases of elderly men.

It is well known that men addicted to exhaustive mental labor and people laboring under worry and anxiety are apt to have precipitates of earthy phosphates in their urine. If to such conditions be added habits of vegetarianism, which tend to depress the acidity of the urine, triple phosphates in addition may readily fall out of solution and form deposits.

CYSTINURIA.

Cystin ($C_3H_6NSO_2$) is comparatively rarely met with as a urinary deposit. Its origin in the economy is not clearly understood, although its highly sulphurous composition (about 25 per cent.), together with its close resemblance in composition to *taurin*, suggest the possibility that the liver may be its source. The discovery of cystin in the livers of typhus patients by Scherer, as well as the discovery of cystinuria in cases of diminished bile secretion by Marowski, would further favor the above view. Stadthagen claims that cystin is absent from normal urine, though Goldman and Baumann succeeded in separating it in very small quantities from healthy urine as a benzoyl compound.

Cystin is a crystalline compound of feeble chemical affinities, and occurs in two forms, (*a*) most commonly in six-sided tablets of variable sizes, and somewhat resembling the six-sided crystals of uric acid. These tablets possess an opalescent lustre,—"*mother-of-pearl*" appearance,—and when traced with fine lines of secondary crystallization, or formed into rosettes, they present microscopical pictures of great beauty. (*b*) The second form of cystin crystals is that of four-sided square prisms, which lie separately or in stellate form. They are highly refractive, and when their sides lie out of the direct line of vision they appear almost black, forming a strong contrast with those sides presented vertically to the light, which appear of a brilliant-white color. Cystin is soluble in the caustic alkalies, oxalic and strong mineral acids. It is insoluble in boiling water, acetic acid, alcohol, and ether.

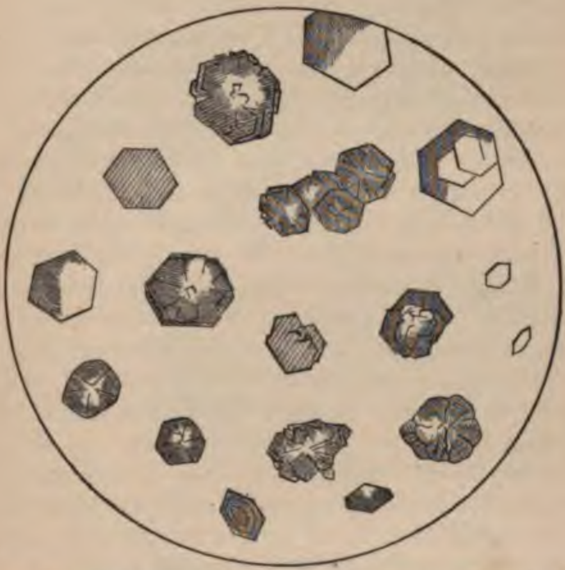


FIG. 18.—THE MORE COMMON FORM OF CYSTIN CRYSTALS. (After Peyer.)

Differentiation.—Cystin may be readily distinguished from the pale, lemon-colored, six-sided crystals of uric acid, as follows: Permit a drop of ammonia to mingle with the deposit on a glass slide, when either form of crystals disappear. Next, evaporate; and if cystin be present the crystals re-appear, showing that they were merely in solution. If, on the other hand, the crystals were uric acid, no re-appearance occurs upon evaporation, but, instead, crystals of ammonium urate appear, showing chemical combination, and not solution.

Another simple method consists in treating the crystals with oxalic or hydrochloric acid, which promptly dissolves cystin crystals, but leaves uric acid unchanged.

From triple-phosphate crystals cystin is readily distinguished by its behavior with acetic acid, the former being immediately dissolved therewith, while cystin remains unchanged.

The urine containing cystin is usually pale in color, of faintly-acid reaction, and upon standing develops the odor of sulphuretted hydrogen, as well as that of ammonium. The sediment is of pale-lemon color, and often changes to green upon standing.

Clinical Significance.—Unfortunately but little at present of a positive nature is known as to the clinical relations of cystinuria. Its frequent association with hepatic disorders may be said to be established. Cystin deposits are said to be results of extensive renal degenerations. Chlorotic women and strumous children are also believed to be prone to cystic deposits in their urine. Ebstein has noted the presence of cystin deposits together with albumin in the urine in cases of acute articular rheumatism. Cystin deposits have been known to occur repeatedly in the same family by a number of independent observers, among whom are Marcet, Lenoir, Civiale, Toel, and Ebstein. Cystin calculus is well known to run in certain families. Cystinuria is said to be most common in young males, although no age or sex can be said to be exempt from it. It may be present and continue for years without any noticeable impairment of health.

The chief interest connected with cystic deposits is their proneness to form concretions of cystin gravel; and although these are comparatively rare occurrences, their consequences are none the less serious when occasionally encountered.

LEUCINURIA AND TYROSINURIA.

Leucin ($C_6H_{13}NO_2$) and tyrosin ($C_9H_{11}NO_3$), as will be seen from their formulæ, are closely related, being products of decomposition of proteid bodies or of their derivatives. Since they are nearly always found associated with each other in the urine, they will be considered together.

Leucin occurs as a urinary sediment for the most part in the form of yellowish, highly-refracting spheres, though not quite so highly refracting as oil-globules, which they somewhat resemble. In a pure state it crystallizes in scales or rosettes, often of irregular shapes, and it has a greasy feel. Leucin is insoluble in ether, which readily distinguishes it from oil-globules. It is also insoluble in mineral acids, but is partly soluble in water and alcohol and is completely soluble in caustic alkalies. For ordinary practical purposes leucin may be known by the microscopical appearance of the crystals, and in this way very minute traces may be determined with certainty. Confirmation by chemical tests may be employed if a fair amount of the material be at hand. (*a*) Thus, solutions heated with proto-nitrate of mercury give deposits of metallic mercury (Hoffmeister). (*b*) When fused with nitric acid on platinum-foil it leaves a colorless residue, which if heated with caustic potassium forms drops of an oil-like fluid which do not adhere to the platinum (Scherer). (*c*) Upon

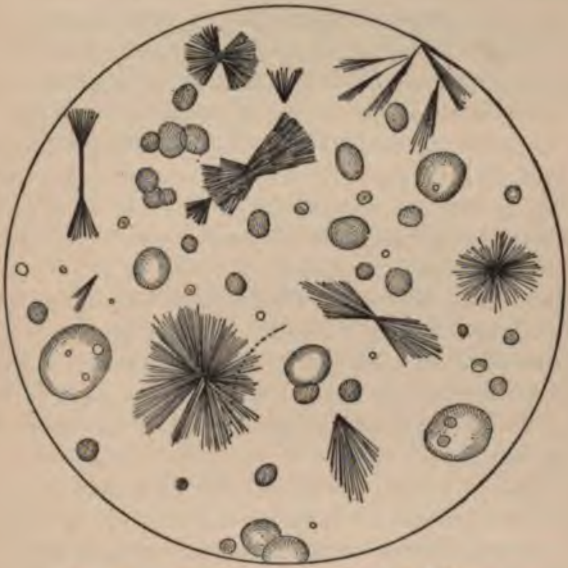


FIG. 19.—LEUCIN AND TYROSIN. (After Peyer.)

heating leucin in a glass tube open at both ends to about 170° C. it sublimes in feathery particles, which float about in the air within the tube. Further heat causes it to fuse and mostly disappear into carbonic acid and amilymin. Leucin may be separated from the urine by evaporating the latter and dissolving the residue in boiling alcohol. Upon cooling the leucin present will be deposited in whitish plates or masses. Leucin is normally present in the liver, pancreas, spleen, lymph glands, salivary glands, and in the thyroid and thymus glands.

Tyrosin crystallizes in the form of very fine needles, arranged in sheaf-like collections. In masses the crystals are snow-white, tasteless, and odorless. If crystallized from an alkaline solution tyrosin often assumes the form of rosettes composed of fine needles arranged radiately (Fig. 19). Tyrosin is insoluble in alcohol and ether, feebly soluble in cold water, readily soluble in acids, alkalies, and hot water. Aside from its crystalline form and characteristic solubilities, tyrosin may be readily recognized by several pronounced reactions.

(*a*) *Hoffmann's Reaction.*—When heated with Millon's reagent, solutions of tyrosin yield a brilliant crimson or pink coloration, which, if much tyrosin be present, is accompanied finally by a similarly-colored precipitate. The test in its original form was applied by heating with a solution of mercuric nitrate in presence of nitrous acid.[1]

(*b*) *Piria's Reaction.*—If tyrosin be moistened on a watch-glass with concentrated sulphuric acid, and warmed for five or ten minutes on a water-bath, it turns pink, owing to the formation of tyrosin-sulphonic acid,—$C_9H_{10}(SO_2OH)NO^3 + 2H_2O$. This is then diluted with water, warmed, neutralized with barium carbonate, and filtered while hot. The filtrate yields a violet color on the careful addition of very dilute perchloride of iron. The color is readily destroyed by an excess of the iron salt.

(*c*) Tyrosin gives out the odor of phenol and nitro-benzol upon heating (Kuhn). Tyrosin may be separated from the urine by first precipitating the coloring matters and extractives of the urine by means of basic lead acetate, then decomposing the filtrate with sulphydric acid and again filtering. Upon evaporating the filtrate to the thickness of syrup, tyrosin crystals will be deposited upon cooling.

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[1] Liebig's Annal., Bd. lxxxvii, 1853, S. 124.

Clinical Significance.—Leucin and tyrosin, as already stated, usually occur together, and this applies both to the urine and the organism at large. Being products of decomposition of proteids, they form in the system in very minute quantities, if at all, during normal metamorphosis. When metamorphic changes of a retrograde nature are rapid, as in extensive suppuration and gangrene, they form in large amounts. They may in such cases pass into the urine, largely supplementing urea.

Leucin and tyrosin are found in the urine in acute atrophy of the liver, in acute phosphorus poisoning, often in very considerable amounts. They have also been observed in the urine in cases of leucocythæmia, typhoid, and small-pox.

MELANURIA.

Melanin is a black pigment which occurs pathologically in the urine under various circumstances. It is insoluble in cold alcohol, ether, acetic acid, and dilute mineral acids. It is soluble in boiling, strong mineral acids, in boiling acetic and lactic acids, and in strong solutions of caustic sodium, potassium, and ammonium.

Melanin contains carbon, nitrogen, iron, and sulphur,—the latter in large amount. The urine containing melanin is not usually dark when voided, but it soon becomes so upon exposure to the atmosphere, and it becomes intensely black if submitted to such oxidizing agents as sulphuric and hydrochloric acids and chloride of iron. Melanin occurs as a urinary deposit in the form of small, lumpy granules, much resembling carbon particles. In the urine it may be detected by several reactions: (*a*) By the addition of bromine-water to urine containing melanin a yellow precipitate is deposited, which gradually blackens. This is considered by Zeller the most delicate test for melanuria. (*b*) When melanotic urines are treated with solutions of ferric chloride, they yield, according to the concentration of the reagent, either a dark-brown cloudiness or else a black precipitate, soluble in excess of the precipitant. This test is both delicate and characteristic. (*c*) When melanin is present in the urine, if treated with a dilute solution of nitro-prusside of sodium and some caustic potassium be added, a pink or red coloration usually appears, which turns blue on the addition of acids, owing to the formation of Prussian blue. The latter reaction is not due to the melanotic pigment, but to some other substance simultaneously excreted.

Clinical Significance.—Melanuria is frequently observed in people who are subjects of pigmented tumors, notably melanotic cancer or sarcoma. It has also been observed in people suffering from repeated attacks of intermittent fevers. The urine of people in wasting diseases sometimes contains considerable deposits of melanin. The practical significance of melanuria, as Jaksch has pointed out, is greatly weakened by the facts that the urine may contain a large quantity of melanin in wasting diseases, while in melanotic cancer or sarcoma the urine may be free from it. For diagnostic purposes, therefore, so far as sarcoma is concerned, it should only be regarded as adjunct.

LIPURIA.

Normal urine contains small amounts of fatty matter, *palmatin*, and *stearin*,—about 2 grains per gallon. It is probable that these neutral fats are increased upon a fatty diet, since numerous cases are recorded in which fat has been found in abnormal quantities unaccompanied by pathological conditions. Fat is soluble in hot alcohol, ether, benzol, carbon disulphide, and chloroform. When mixed with colloids in an alkaline solution, fat is broken up into fine globules, becoming white like milk,—an emulsion. Under the microscope fatty sediments appear in the urine in the form of highly-refracting globules of various sizes, with dark and somewhat irregular margins. If the urine contain fat in considerable quantity, it is usually of a milky color, but this readily clears by shaking it with ether.

Clinical Significance.—Small quantities of fat are frequently met with in the urine in chronic parenchymatous nephritis, in fatty changes in the kidneys, in phosphorus poisoning, and in diabetes mellitus. In one case of diabetes mellitus the author met with a large amount of fat in the urine, the occurrence of which was intermittent, alternating with the appearance of sugar.

Ralfe also states that he found an abundance of oil-globules in the urine of a patient who died of diabetic coma. Ebstein found a large amount of fat in the urine in a case of hydronephrosis. Lipuria is a physiological condition with pregnant women. Roberts has recorded several cases in which pure oil appeared in the urine after the administration of codliver-oil. Henderson has reported three cases of lipuria associated with heart disease.

In diseases of the pancreas lipuria is not uncommon, and in such cases lipuria has appeared before oil was to be noted in the stools. Fat is also frequently observed in the urine after fracture of bones and during the course of repair. In acute yellow atrophy of the liver, followed by fatty changes in the renal epithelium, the urine contains an excess of fatty matters.

In chyluria the urine contains a large amount of fatty matters as well as albumin and blood-corpuscles. The features of this disease, however, will be fully considered in a future section of this work.

SECTION VII.

ANATOMICAL SEDIMENTS.

HÆMATURIA.

Blood-corpuscles appear as a urinary sediment in a number of conditions, all of which are pathological. Their appearance varies according to the character of the urine in which they are found, and the location of the tract from which they exude. The typical microscopical appearance of blood-corpuscles is so characteristic that little difficulty is encountered in distinguishing them from all other urinary sediments (Fig. 20). Their original form is that of biconcave discs of yellowish color. In focusing with the fine adjustment of the microscope, the margins of the corpuscles undergo reversal of light and shade owing to their biconcave form. Blood-discs are distinguished from pus-corpuscles by the absence of visible cell-contents and nuclei of the former.

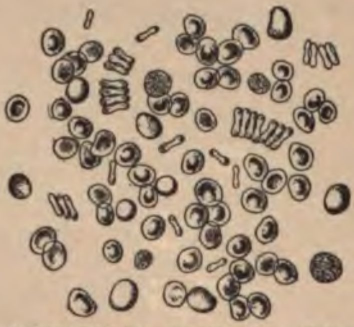

FIG. 20.—NORMAL BLOOD-CORPUSCLES. (After Peyer.)

In acid urine blood-corpuscles long retain their characteristic features, although in time they shrivel somewhat, and become dentated at their margins—more or less stellate in form. In urine they do not, as a rule, tend to run together, or to form rouleaux as when drawn from a blood-vessel, but are for the most part distributed pretty evenly over the field of vision. Exceptions to this rule sometimes occur in cases of pronounced hæmorrhage from the bladder or urethræ.

If the urine be concentrated the biconcave character of blood-corpuscles becomes exaggerated, but the corpuscles shrink somewhat and are more apt to become indentated or jagged at their margins. On the other hand, if the urine be dilute—*i.e.*, of low specific gravity—the corpuscles swell and become biconvex, or even spherical, and at the same time they lose their optical characteristics as well as their coloring matters. This occurs the more readily if the urine be ammoniacal.

The urine containing blood is usually cloudy and more or less reddish in color, according to the quantity present. If the quantity of blood be considerable and the urine be acid the color is dark red, but if the urine be alkaline the color is bright red. If the quantity of blood in the urine be small the color may give no indication of its presence, especially if the urine be concentrated. Generally speaking, if the blood come from the kidneys it is diffused evenly through the urine, imparting to the latter a reddish, hazy tint. If, on the other hand, the blood be derived from the lower urinary tract, the color is usually bright, and clots are not infrequently present. Lastly, if blood appear in the urine in quantities however small, a distinct albuminous reaction is always obtainable.

Clinical Significance.—The clinical significance of hæmaturia embraces a very wide and varied class of pathological conditions. In order, therefore, to afford any practical information it must first be determined from what source the hæmaturia arose.

In hæmorrhages *from the kidney* the urine is usually of an homogeneous, reddish-brown color, of acid reaction, of lowered specific gravity, and it often contains renal casts and renal epithelium. After standing the urine deposits more or less brown, coffee-colored sediment. If pyelitis be present, the urine may have an alkaline reaction. In hæmaturia of renal origin clots are usually absent from the urine, unless they be of the long, slender, rod-like variety, showing that they have been molded in passing through the ureters. The recognition of blood-casts in the urine forms the most conclusive proof of the renal origin of hæmaturia. The most frequent cause of renal hæmaturia is the class of renal diseases grouped together under the term of Bright's disease. In the acute forms of these lesions hæmaturia is nearly always present. The hæmorrhage is not very pronounced in these cases, being of parenchymatous origin. It usually subsides with the more acute symptoms of the disease. Of the chronic Bright's lesions the interstitial form is the most frequent cause of hæmaturia, and in such cases the hæmorrhage is the most pronounced and obstinate of all renal hæmorrhages, except that from malignant and cystic disease of the organs. This is due to the accompanying vascular changes, including cardiac enlargement and atheromatous arteries.

Amyloid disease less frequently gives rise to hæmaturia, although it is by no means rare in such cases, since the small renal vessels in this disease undergo pronounced degenerative changes. In chronic diffuse inflammatory lesions of the kidney hæmaturia is almost unknown.

Malignant growths of the kidney give rise to most troublesome, profuse, and repeated attacks of hæmaturia. Such cases are to be recognized by renal tumor, pain, and general cachexia of the patient. Tubercular disease of the kidney not infrequently gives rise to hæmaturia. The urine in such cases contains more or less pus and broken-down tissue *débris* which do not altogether subside as a sediment. Hæmaturia from tuberculosis, like in cancer, is intermittent in character, and there may also be present tumor, but usually no pain. The diagnosis rests upon the general symptoms of tuberculosis, such as emaciation, elevation of temperature, etc.; but most conclusively upon the isolation and propagation of the *bacillus tuberculosis* from the urine.

Renal calculus, whether confined to the kidney or, as is more frequent, when occupying the renal pelvis, nearly always gives rise to hæmaturia sooner or later. In these cases the hæmorrhage is most marked upon exercise, and usually diminishes or subsides upon continued rest. Pus-cells are always present in the urine in hæmaturia of calculous origin. Fixed pain in the region of the kidney, usually with tenderness upon deep pressure over a certain point, sometimes retraction of the testicle as well as reflected pain upon the affected side, often extending down the leg, serve to diagnosticate hæmaturia of calculous origin.

In endemic hæmaturia of the tropics the cause is due to a minute parasite in the kidney—*Bilharzia hæmatobi*—which will be described later on. Among the other causes of hæmaturia of renal source may be mentioned cystic disease of the kidneys, abscess, renal embolism, hydatids, acute febrile processes, purpura hæmorrhagica, uterine and crural phlebitis. Renal hæmaturia may arise from the ingestion of certain drugs, as turpentine, cantharidis, and a number of toxic substances. Lastly, hæmaturia of renal origin may arise in consequence of traumatisms involving the kidneys, either directly as by blows or wounds, or indirectly from concussion.

In *vesical hæmaturia* the urine is usually alkaline in reaction, always so if accompanied by cystitis of long standing. In such cases the urine is ammoniacal and thick from muco-pus, and crystals of triple phosphate are usually present. In vesical hæmaturia clots are more common than in other forms of hæmorrhage. These are usually of an irregular or ragged shape. The blood is brighter in color and less intimately mixed with the urine than in hæmaturia of renal origin. Stone in the bladder is perhaps the most frequent cause of hæmaturia of vesical origin, and, in such cases, the blood is almost normal in appearance and is passed mostly at the close of the act of micturition. The grade of hæmaturia in these cases depends largely upon the acuteness of the attack. In cystitis of the vesical neck the symptoms closely resemble those of stone. The most pronounced hæmaturia of vesical origin is that associated with villous growths and carcinoma of the bladder-walls. The urine is usually normal in quantity and specific gravity in such cases, and the reaction is usually feebly acid. The sediment is brownish red, flocculent, and often contains flesh-colored fibres and shreds. The quantity of blood may be so pronounced in these cases as to cause coagulation within the bladder, or, as is more frequent, shortly after the urine is voided. Vesical hæmaturia is also common with neoplasms of the organ, fibrous tumors, polypi, and varicose conditions of the vesical neck.

Hæmaturia of urethral origin may be known by the hæmorrhage preceding the flow of urine as well as between the acts of micturition, the urine itself being usually unaltered in any of its essential characters. It may arise from acute gonorrhœa, neoplasms, traumatisms, urethral chancre, or from surgical operations such as cutting or divulsion of strictures.

PYURIA.

Pus may be derived from any part of the urinary tract and appear in the urine as a sediment. The urine containing pus is always more or less turbid when voided, and gives the albuminous reaction. In their normal state pus-corpuscles appear under the microscope as circular, pale, finely-granular discs, averaging in size nearly double that of the red blood-corpuscle. They contain distinct nuclei, which are often multiple,—two or three. If pus be diluted with water, the corpuscles may be observed to slowly swell up and become paler, with more delicate outlines. This process is more quickly produced by acetic or other organic acid, which renders the nuclei very distinct, but causes the granulated appearance of the cell-protoplasm to disappear (Fig. 21).

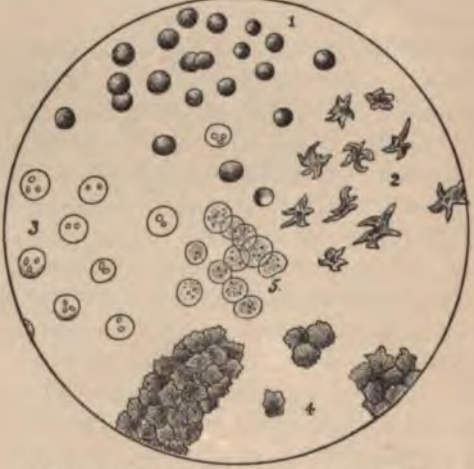

FIG. 21.—PUS-CORPUSCLES. (After Ultzmann.)

1. Normal corpuscles. 2. Pus-corpuscles with prolongations showing amœboid movements. 3. Pus-corpuscles with nuclei rendered distinct by acetic acid. 4. Pus-corpuscles altered by chronic pyelitis. 5. Pus-corpuscles swollen by ammonium carbonate.

Pus-corpuscles are similar to, indeed practically identical with, mucous corpuscles, the white corpuscles of the blood and lymph. When examined in the fresh state they exhibit the amœboid movements, and also show the usual glistening appearance of living protoplasm. As seen in the urinary sediment, pus-corpuscles are dead, the protoplasm being coagulated into coarse granules.

The chief constituents of pus-corpuscles are albuminous bodies, of which the largest proportion is nucleo-albumin, which is insoluble in water, and which expands into a tough, slimy mass when treated with sodium-chloride solution. This substance is soluble in alkalies, but quickly changed thereby into Rovida's *hyaline substance.* Besides this pus-corpuscles contain an albuminous substance which coagulates at 49° C., as well as serum-albumin and peptone. The cell-protoplasm also contains, in addition to the above, *lecithin*, *cholesterin*, *xanthin bodies*, *fat*, *soaps*, *and cerebrin.* In pus from congested abscesses which have stagnated some time there is *peptone*, *leucin*, and *tyrosin*, free *fatty acids* and *volatile fatty acids*, such as *formic acid*, *butyric acid*, *valerianic acid. Pyin* also is a specific constituent of pus,—a nucleo-albumin precipitable by acetic acid.

Pus may be derived either from the free mucous surface of the urinary tract, an ulcer, or from tissue-substance, and in each case it is likely to be mixed with elements from its place of origin which become of great diagnostic value. In addition to this pus-corpuscles themselves frequently contain micro-organisms which explain the pathological conditions of the parts from whence they are derived. Pus-corpuscles are greatly changed by contact with potassium or ammonium; the corpuscles swell up and coalesce into an homogeneous, sticky mass, in which all but the nuclei are indistinguishable by the microscope. Ammoniacal urine containing pus deposits a vitreous-looking, slimy mass, so sticky that in decanting it from a vessel it slips out *en masse.* The peculiar behavior of pus with caustic alkalies just alluded to forms the principle of Donnes's test for pus, by which the latter may usually be known without recourse to the microscope. The test is performed as follows: After the sediment has settled to the bottom of the glass or test-tube, pour off the supernatant urine and add liquor potassæ to the deposit. If the sediment be pus it is at once converted into a glairy, gelatinous-like substance which adheres to the glass or flows in a mass.

The turbidity of the urine containing pus, as well as the sediment itself, often resembles that due to the pale, granular urates. The distinction, however, is easy, since heat dissipates the turbidity due to urates, while it only serves to increase the cloud due to the presence of pus by coagulating its contained albumin. The pus-deposit also frequently resembles the earthy phosphatic sediment, but the distinction here is also easy. The addition of an acid promptly dissolves the phosphate deposit, while it only increases the turbidity due to pus by coagulating its contained albuminous elements.

Clinical Significance.—Of all sediments met with in the urine that of pus is the most common. Any affection of any part of the urinary tract, from the slightest forms of irritation up to the gravest lesions, are usually accompanied by pyuria. The clinical significance of pyuria, therefore, embraces a wide range of pathological conditions.

The first point to be determined, if possible, is to locate the particular field of the urinary tract from whence the pus originated. This may often be determined by the general characters of the urine, together with the nature of the accompanying deposits. When pus originates from the kidney or renal pelvis the urine is most apt to retain its normal acidity. Round epithelium and even casts may be present, and if so it gives the most conclusive evidence of the source of the pyuria, especially the presence of casts. When the pyuria has its source in the kidney or renal pelvis the pus is intimately mingled with the urine when voided, but it quickly settles upon standing, forming a whitish, flocculent sediment. The absence of bladder symptoms in pyuria goes far toward establishing the renal source of pyuria.

Pyuria is usually associated with such renal lesions as chronic diffuse inflammations, pyonephrosis, pyelonephritis, cancer, tuberculosis, and nephritic abscess. In pyelitis, either of calculous or obstructive origin, pyuria is always a prominent accompanying symptom.

When pyuria is of vesical origin the urine is often alkaline—

ammoniacal—when voided; if not, it soon becomes so upon standing. The urine is likely also to contain considerable mucus; so that the deposit is more glairy and sticky than in renal pyuria. In addition to pus the urine is likely to contain such associated deposits as amorphous and triple phosphates and flat epithelium in excess from the bladder-walls. Local symptoms such as frequent and painful micturition aid in pointing to the source of the pus-formation.

Cystitis of all grades is always associated with pyuria, and the quantity of pus-deposit in these cases is often pronounced. Obstructive cystitis, vesical stone, ulceration, tuberculosis, and, in short, all bladder affections are ordinarily associated with pyuria.

In uncomplicated diseases of the prostate pus appears frequently in the urine, often in the form of threads long drawn out. Somewhat similar threads of muco-pus appear in the urine in chronic gonorrhœa. These are often rolled into little balls by the stream of urine as it flows down the urethral canal. The pyuria in acute gonorrhœal conditions is almost self-evident as to its source. If any doubts arise upon the question they may be readily settled by directing the urethra to be flushed, when the urine voided immediately after will be free from pus, if of urethral origin.

Determination of Blood and Pus in the Urine.—When, as is frequently the case, the urine contains a very considerable quantity of blood or pus, it is of practical importance to be able readily to determine the amount of either from day to day, in order to estimate the results of treatment. This may be rapidly accomplished by means of the author's percentage tubes and centrifuge. The process consists simply in sedimenting the urine in the percentage tubes until the urine is clear, the sediment being completely packed in the tips of the tubes, when the bulk percentage may be read off from the scale.

EPITHELIUM.

Epithelium from some part of the urinary tract usually forms a part of every urinary deposit, and, furthermore, it is usual to find scattering epithelial cells in the urine when the latter is in all respects normal. Epithelium is the normal product of mucous surfaces, and may be expected to be found in small amounts in any given sample of healthy urine. But in diseased states of the urinary tract the lining epithelium is often thrown off in very considerable amount, forming plainly-visible urinary sediments.

It was formerly believed that the various divisions of the urinary tract possessed their own special forms of epithelium, and, therefore, the special forms of epithelial cells found in the urine became valuable aids in locating the seat of lesions of the urinary tract. This view is, indeed, still held by a number of prominent observers. More accurate and extensive observations, however, have shown that this can only be depended upon in a very general way. Very often the epithelium claimed to be characteristic of certain divisions of the urinary tract has been found in all its typical peculiarities in a totally different location. This, however, is the more likely to be the case in divisions most nearly located to each other. The divergent views upon this point, held even by the ablest and most experienced observers, may be illustrated by the following: Sir William Roberts describes the epithelium shed from the renal pelvis as that of "very irregular, spindle-shaped, tailed, three-cornered, elongated, rudely circular, etc." Dr. Dickinson has carefully figured the epithelium taken from the bladder, and, in reply, laconically observes: "It will be seen that these varieties of form, even to the *et cætera*, are equally characteristic of vesical disease."

The epithelium in the urine may be classed under three divisions (Fig. 22): (*a*) Small round cells, spheroidal, finely granular, with comparatively large nuclei and nucleoli, the latter excentrically located. They occur singly or collected into groups; in the latter case often cohering rather firmly, so that they float about in masses. They sometimes contain fatty matter, when springing from long-diseased locations. These cells may be found in their most typical form in the convoluted tubes of the kidney. They also occur in the deep layers of the mucous tract of the renal pelvis, bladder, and male urethra. These cells are to be distinguished from pus-cells by their somewhat larger size, larger and more distinct *single* nucleus, requiring no acetic acid to develop or bring the nucleus into view. No positive conclusions can be drawn from the mere appearance of these cells in the urine in reference to the precise location from which they originated. It may be the kidney, renal pelvis, ureter, bladder, urethra, or urethral glands. If, in a given deposit, the round cells in their typical form greatly predominate, and if the urine contain albumin and there be other evidences of renal disease, it may be inferred that the cells come from the kidney. (*b*) The second form of epithelium met with in the urine is the columnar variety. These cells are of irregular, though always elongated, form. They are described as caudate-, spindle-, and cylindrical-shaped. They are inclined to angularity in outline, and, like the round cells, have a well-marked nucleus, visible without the action of reagents. They may occur singly or in groups. The columnar epithelium may be derived from the superficial layer of the mucous membrane of the renal pelvis, or from the deep layers of the bladder, ureters, or urethra. The statement of Ebstein,[1] that tailed epithelial cells associated with pyuria constitute the most positive evidence of pyelitis, is quite untenable. More recent and accurate observation has amply demonstrated that these cells exist in all their typical forms throughout the whole urinary tract, excepting the kidney itself. (*c*) The third variety of epithelium met with as a urinary sediment is the

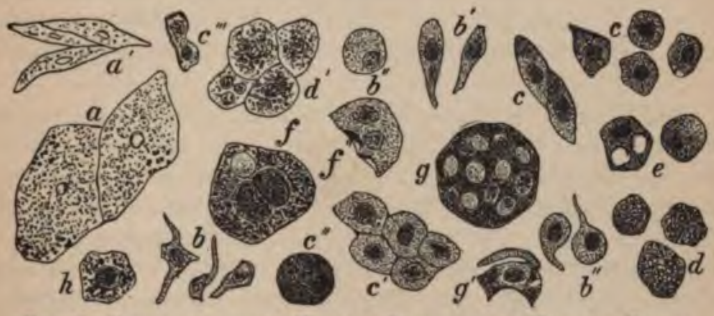

FIG. 22.—EPITHELIUM FROM VARIOUS PARTS OF THE URINARY TRACT. (After v. Jaksch.)

a, *a*′, squamous epithelium; *b*, *b*′, *b*″, epithelium from the bladder; *c*, *c*′, *c*″, *c*‴, epithelium from the kidney; *d*, *d*′, fatty epithelium from kidney; *e* to *h*, epithelium from the bladder.

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[1] Von Ziemssen's Cyclopædia of Medicine, vol. xvi, p. 574.

squamous or pavement form. These cells are large, flat, somewhat rounded, though irregular in outline, and have a distinct and usually central nucleus, very prominent without the aid of reagents. These cells are derived chiefly from the bladder and vagina; in the latter case the cells are usually larger than those from the bladder.

Clinical Significance.—As already stated, little more than inferences are to be drawn from the appearance of a particular form of epithelium in the urine, as to the precise location of its origin. While certain forms of epithelium predominate upon the superficial surface of the mucous tract in certain locations, the deeper layer always contains transition cells, which approach more nearly those of the surface layer in other locations. In diseased conditions, therefore, cells are thrown off from both the surface and deep layers, and the epithelium is nearly always, accordingly, of mixed varieties.

But if we are unable to locate the anatomical seat of a lesion by the character of the deposited epithelium, we may, nevertheless, gather information of value as to the nature of the pathological condition present from the exfoliated cells found in the urinary sediment. With regard to renal lesions, it may be stated that practically the whole class of so-called Bright's lesions are attended by epithelial sediments in the urine. In the acute diffuse inflammations of the kidney the round epithelial cells from the urinary tubes are often thrown off in large quantity, so as to form a very considerable sediment. For the most part, in such cases, the epithelium is in a good state of preservation, the nuclei and outlines of the cells being sharply marked. In the more chronic lesions of the kidney the round epithelium appearing in the sediment is often fatty, the space between the nuclei and cell-walls being sometimes filled with oil-globules. The cells themselves are often partly disintegrated or broken down, presenting a ragged appearance. These partly-disorganized cells may often be seen adhering to renal casts, or they may themselves become adhered together, forming casts.

In chronic interstitial nephritis and uncomplicated amyloid disease of the kidneys but little desquamation from the renal tubules occurs, and in these cases the fewest round cells occur in the urine. On the other hand, in acute scarlatinal nephritis the number of round epithelial cells in the urine is sometimes enormous. In acute congestive conditions of the kidney a very decided deposit of round cells are sometimes met with in the urine, without other pronounced changes in the latter save albuminuria.

In pyelitis and diseases of the renal pelvis considerable deposits of epithelium are met with, and in such cases, although round cells may be present, the tailed and spindle-shaped cells—columnar—are more apt to predominate.

In cystitis there is more or less deposit of large flat epithelium. If the cystitis be of mild grade or largely confined to the superficial surface of the mucous coat of the bladder, the large, flat, irregular-shaped epithelium predominates, but in cystitis involving the deeper layers the large flat cells are more likely to be mingled with the columnar variety.

URINARY CASTS.

Urinary casts have always and very properly been regarded of the highest diagnostic value. They were probably first seen by Vigla and Rayer, but the able investigations of Henle and Rovida gave to the profession the most complete information as to their character and significance.

Three chief views have been held as to their nature and mode of production :—

First, that they are the result of disintegration of the epithelium of the renal tubules, the resulting products becoming packed into molds by the pressure of urine, until at length they slip through the smaller convoluted into the large straight tubes and appear in the urinary sediment.

Second, that they consist of a secretion of the morbidly irritated epithelium lining the renal tubules, which become caked into molds and are washed down with the urine.

Third, that they consist of coagulable elements of the blood which gains access to the renal tubules through pathological lesions of the latter, and that any free or partly-detached products of the tubules become entangled in this coagulable product, assisting to form the molds of the tubules, which subsequently appear in the urine as casts.

The last view is the one most generally accepted, at least so far as the nature and origin of the great majority of casts are concerned.

Although the substance forming the basis of casts is evidently closely allied to proteids, yet it is certain that it is not identical with any proteid with which we are at present familiar; perhaps it is a derivative thereof. Rovida claims for hyaline casts the characteristic of being soluble in dilute mineral acids. Renal casts have been variously classified, but the most useful division for clinical study is as follows:—

1. Those consisting of anatomical elements such as epithelial cells, blood- and pus- corpuscles.

2. Those consisting of the products or broken-down elements of anatomical substances.

3. Those clear casts often termed "*hyaline*," the nature of which, as well as is their origin, is still a disputed question.

The first division naturally includes those casts largely made up of (*a*) red blood-corpuscles, (*b*) leucocytes, (*c*) epithelial cells, (*d*) masses of bacteria.

The second division comprises (*a*) granular casts, (*b*) fatty casts.

The third division comprises (*a*) narrow hyaline casts, (*b*) broad casts, (*c*) composite casts or those largely clear, but more or less coated with the elements enumerated in the first and second divisions, such as blood, pus, epithelium, fat, etc.

Blood-Casts.—These appear in the urine under conditions which give rise to hæmorrhage within the urinary tubules. Under the microscope they often appear as very beautiful objects. The perfectly-preserved corpuscles may be observed glued together in perfect molds of the tubules, being usually short, of pretty uniform diameter throughout, and with rounded ends.

These casts are met with in the urine in hæmaturia, acute diffuse nephritis, acute renal congestion, and hæmorrhagic infarctions of the kidneys. Blood-casts do not in themselves furnish positive evidence of organic renal disease, since any hæmorrhage of the kidney may have associated therewith blood-casts in the urine. On the other hand, it may be stated that the presence of blood-casts in the urine constitutes the only positive evidence of the existence of renal hæmorrhage. Blood-casts may be considered as belonging to the rarer forms of renal casts found in the urine, and they are usually difficult to find, since a large sediment of free blood-corpuscles usually accompanies them, which greatly obscures the microscopical field.

Epithelial Casts.—These result from pathological conditions which cause exfoliation of the epithelium of the renal tubules. Sometimes the epithelial lining of the tubules is thrown off intact for short distances, resulting in epithelial cylinders which possess lumens. The epithelial cast also occurs in a solid form, the body being made up of hyaline substance and the surface covered with epithelial cells. These cells, as viewed under the microscope, appear more or less swollen and granular, with ill-defined margins. In some cases the epithelial cells appear in rows or in patches over the surfaces of the casts (Fig. 23). In other cases the

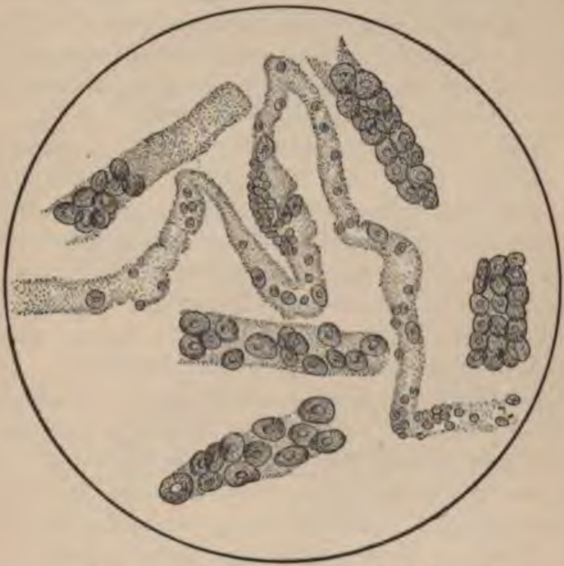

FIG. 23.—EPITHELIAL CASTS. (After Peyer.)

epithelial cells have partly undergone degeneration or contain dotlets of fat. These are significant of chronic or, at least, fatty changes in progress in the kidney. Finally some casts are to be seen which are entirely composed of epithelial cells agglutinated together. Epithelial casts are usually of medium size and length, refracting light to a comparatively high degree, and are therefore easy to discover in the microscopical field. They resist the action of chemical reagents to a greater degree than most other casts, except those that are partly metamorphosed. The presence of epithelial casts in the urinary sediment may be taken as a positive evidence of inflammation in the anatomical structures from whence they originate; and they are consequently sediments of the highest diagnostic value.

Pus-Casts.—Casts composed exclusively of pus-corpuscles are exceedingly rare. Not infrequently, however, compound casts are met with, composed of epithelium or granular matter, in which scattering pus-corpuscles may be seen dotted over their surfaces. Johnson has described and illustrated casts entirely composed of pus-corpuscles which came from subjects who subsequently died of multiple abscess of the kidneys. Such casts, however, have rarely been noted by other observers.

Bacterial Casts.—It is no rare occurrence to meet with casts in the urine which are composed of masses of micrococci. In appearance they closely resemble the dark granular casts, but they are readily distinguishable from the latter by their resistance to such chemical agents as strong mineral acids and caustic alkalies. They are more opaque than other casts, of a grayish color, and are uniform and very fine in their outlines. The use of high microscopical powers will render confusion in distinguishing these casts almost impossible. The discovery of casts in the urine made up of bacterial masses must be taken as a factor of very grave significance, since they are chiefly found in septic forms of nephritis often accompanied by embolism. They occur, therefore, in interstitial suppurative nephritis or ascending pyelonephritis.

Granular Casts.—This form of renal cast comes under the second division named, being the result of metamorphosis of anatomical elements, usually of epithelium, pus, or blood. Granular casts are found in the urine in great variety, as is shown by the terms frequently employed to designate them, such as *finely granular*, *coarsely granular*, *granular*, *highly granular*, *moderately granular*, *light granular*, *dark granular*, etc.

Granular casts vary much in size and shape, as well as in appearance. They are most often met with in fragmentary forms, only occasionally preserving their entirety or perfect forms. They are irregular both in their coarse and fine outlines, and their ends are usually ragged, as if recently fractured. The granulations are often exceedingly fine, requiring high powers to distinguish them; while, again, they are *coarsely granular*, which is apparent with comparatively low powers (Fig. 24). They are of various colors, as yellowish, white, gray, and brown. They may have scattered over their surfaces epithelium, leucocytes, fat-globules, or fatty crystals. Granular casts have generally been regarded as indicative of pathological conditions of the kidneys of chronic or degenerative character.

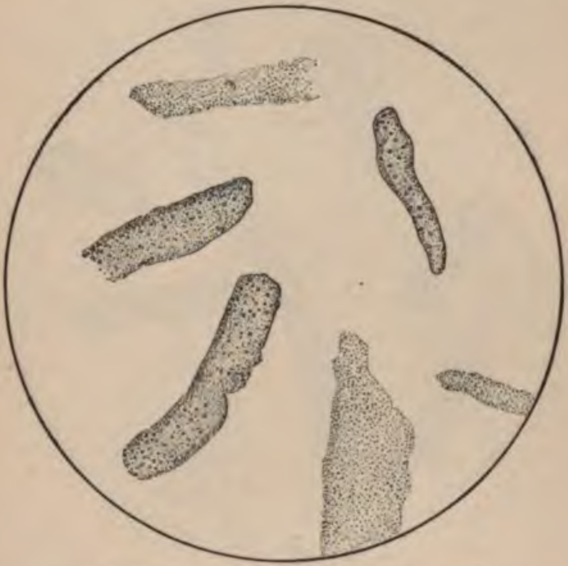

FIG. 24.—GRANULAR CASTS. (After Peyer.)

Fatty Casts.—It has already been stated that fatty elements are sometimes seen mingled with the elements of epithelial casts, and the same may be said with regard to granular and many other forms of casts. But, in addition to these, highly-refracting casts are often met with in the urine, whose surfaces are completely studded over with fatty globules and, less often, with fine, needle-like, fatty crystals (Fig. 25). Fatty casts are the result of a different form of transformation of anatomical elements from the last described. They constitute the index of fatty changes in the kidneys, and are found in their most typical form in "large white kidney." They may be looked upon as evidences of pathological states of the kidney, the chief feature of which is extreme chronicity, since they are probably the result of complete destruction of the cell-protoplasm, which becomes replaced by fatty elements.

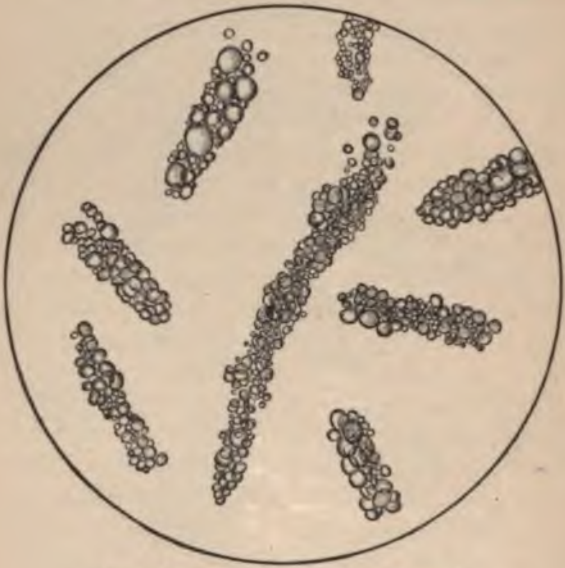

FIG. 25.—FATTY CASTS. (After Peyer.)

Hyaline Casts.—These are pale structures of variable but usually considerable length, sometimes very difficult to detect in the sediment (Fig. 26). Sometimes they exhibit no granulation whatever upon their surfaces, being, in fact, almost transparent. Much more frequently, however, they exhibit very fine granulation of a very light color. They may exhibit here and there a dotlet of oil or a fragment of epithelium upon their surfaces, and, indeed, this is usually the case, although such casts are considered strictly of the hyaline order.

With regard to the origin of hyaline casts, much difference of opinion has prevailed. Oertel contended that they were the result of secretion from the epithelial cells of the renal tubules, and in this opinion he was supported by Rovida. Bartels, on the other hand, holds that these casts are formed by a coagulation of the albumin or its derivatives excreted with the urine. As evidence of this, he states that they are only present in urine that is albuminous, or that has very recently been albuminous; for the occurrence of albuminuria and casts are not always simultaneous.

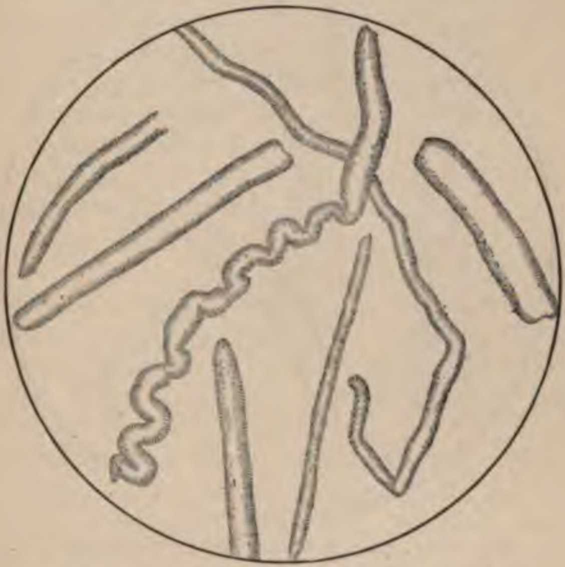

FIG. 26.—NARROW HYALINE CASTS. (After Peyer.)

While the origin of the hyaline casts is not at present so clearly understood as most of the other forms, it is probable that they are formed by coagulable elements of the blood which has gained access to the renal tubules. The experiments of Ribbert upon animals indicate that hyaline casts may result directly from exudation of albumin into the tubules; and their disappearance from alkaline urine upon standing further indicates their close relationship to albuminous bodies, as long since demonstrated by the author.[1]

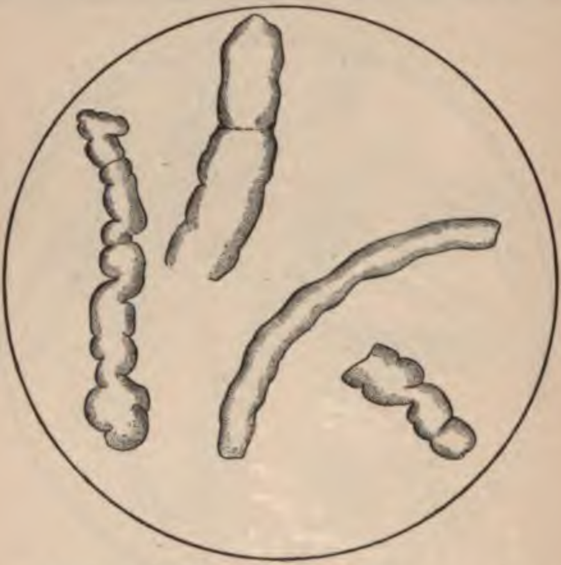

FIG. 27.—SO-CALLED WAXY CASTS. (After Peyer.)

Numerous observers have claimed to have found hyaline casts in non-albuminous urine, but the author agrees distinctly with Bartels in that he has never met with them save in albuminous urine or urine that has recently been albuminous.

The disposition by some to regard hyaline casts of the small, narrow order as of no serious import is a mistake of the gravest character, for, indeed, they are often the chief evidence, so far as the urine is concerned, of the existence of a most serious form of renal disease, viz., interstitial nephritis; for it should be remembered that in such cases albuminuria is nearly always small in quantity.

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[1] Journal of the American Medical Association, September 12, 1885.

In addition to narrow hyaline casts which doubtless come from the smaller tubules within and above the middle zone of the kidney, the urine often contains large; broad hyaline casts, evidently emanating from the large, straight tubes of the pyramids. As a rule, these larger, clear casts are more refracting, and consequently more distinct both in body and outline than the narrow casts. They are also more indentated at their margins, although pretty uniform in their dimensions. There is a form of hyaline cast, usually of large size, that occasionally—not always—exhibits the characteristic amyloid reaction with methyl-violet and iodo-potassic iodine solutions. They are large and usually rather long, and their surfaces may be marked by indentations showing imperfect vertical segmentations,—"*tape-worm form*" (Fig. 27). The term *waxy* as applied to these casts is inappropriate. It was formerly thought that these casts were characteristic of amyloid changes in the kidneys, but more extended observations have shown that they are found in all forms of nephritis. "These casts may exhibit the amyloid reaction in the absence of amyloid kidneys, or they may fail to exhibit it when amyloid disease of the kidney is present, and therefore no diagnostic value can be attributed to the reaction, save, perhaps, as indicating degenerative changes in the casts themselves" (Roberts). These casts are of comparatively rare occurrence.

Cylindroids.—In addition to the casts described, the urine sometimes contains the so-called cylindroids of Thomas, who first observed them in the urine in a case of scarlatina. These are long, wavy, ribbon-like structures, which often divide and subdivide at their ends with diminishing diameters. These ends may be folded or twisted in corkscrew form. They are pale, colorless, and of greater length than the ordinary casts described, and rarely, if ever, have attached to them any cellular elements whatever. They appear flat and do not give the impression, to the eye, of being solid structures like true renal casts. It seems not improbable, however, that these cylindroids come from the renal tubules. They occur in nephritis, cystitis, and renal congestion, and may be present in urine that is free from albumin. They are not characteristic of kidney disease, but probably more often caused by irritation of the lower urinary tract, which has, in a measure, extended to the kidneys.

Lastly, it may be stated that casts are sometimes met with in the urine composed of urinary crystals or granular salts. Only those composed of urates and hæmatoidin have thus far been observed, and they are of little practical significance, being only found in the urine of infants, or in cases of gout, renal congestion, etc.

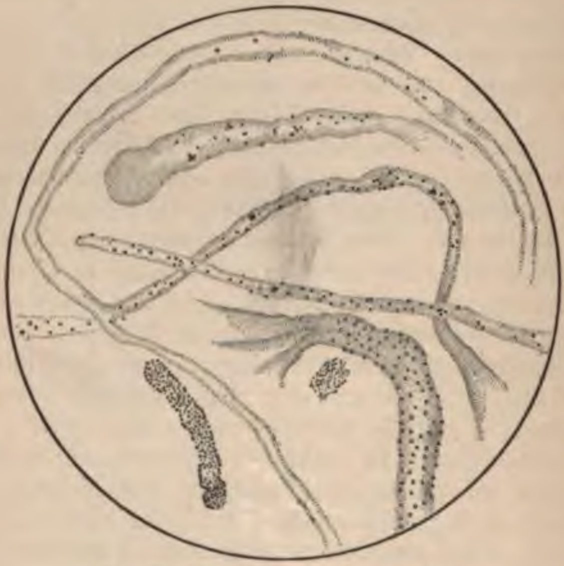

FIG. 28.—FALSE CASTS. (After Peyer.)

Method of Searching for Casts.—Since the more recent methods of obtaining the urinary sediment by means of the centrifuge, we no longer encounter the obstacles which were often very annoying and sometimes almost impossible to surmount in making a satisfactory microscopical inspection of the urine. The obstacles referred to especially were the following:

(*a*) The difficulty often encountered in getting casts to settle in urines of high specific gravity, because renal casts are of comparatively light weight and often float in such urines for hours without subsiding. (*b*) The changes in the urine upon standing often altered the essential features of the deposit, as before stated, sometimes rendering them unrecognizable. (*c*) In urine which stood long enough to secure the sediment, the microscopical field sometimes became so crowded with micro-organisms that the organic products were completely obscured from vision. Happily, these difficulties are now matters of the past; and it is only necessary to secure a freshly-voided sample of urine, submit it to the centrifugal apparatus for two or three minutes, and we have a true and unaltered sediment, that exactly represents the pathology of the urine as it leaves the urinary tract.

The urinary sediment obtained—always preferably by the centrifuge—is best examined in a shallow cell, upon a glass slide carefully covered with a cover-glass. This is best secured by taking up about 4 to 6 drops of the sediment in a nipple-pipette from the bottom of the sediment-tubes of the apparatus, and placing them upon a carefully-cleaned slide, then placing the cover-glass over the cell, and with the thin, freshly-torn edge of a piece of blotting-paper removing the excess of urine, which tends to spread over the cell and along the slide. By this means the sediment constitutes a temporary mount, so that it may be examined at any angle without flowing out of the cell. The slide is next placed under the microscope, which is adjusted with a ¼-inch objective for ordinary search, and examination conducted in a clear, but not too bright, light.

The greatest difficulties encountered in searching for casts in the urine will usually be met with in the case of narrow hyaline casts. These bodies are so transparent and non-refracting that they are exceedingly liable to be overlooked. This may often be avoided by proceeding as follows: After securing an accurate focus of the field by careful regulation of the fine adjustment of the instrument, gradually darken the field by the mirror-adjustment and throw the light obliquely across it, illuminating the field, in fact, but about one-half or two-thirds its extent. Next, by slowly moving the slide about, the different features of the sediment are presented to view in different lights, and the outlines or shadows of fine hyaline casts will often be brought into view, when they would be perfectly transparent and unobservable in a more direct reflection of sharp light. Once the outline is seen, by careful re-focusing the cast often stands out with distinctness. If doubts remain as to its true nature, by depressing both ends of the slide with the finger-tips currents will be created in the urine beneath the cover-glass (if mounted as directed), so that the cast will be made to move and even roll over, which will often settle any question as to its nature. The author has not found it necessary to treat these casts with staining agents to bring them into view, although this may be practiced successfully. It is, however, preferable, if possible, to view the microscopical deposit, and especially renal casts, as nearly as possible in their native state, for obvious pathological reasons.

SPERMATOZOA.

Spermatozoa are thread-like bodies provided with a head and a long, tapering, tail-like extremity. The head is of a flattened oval shape with a central depression on either side. The head and tail are united by an intermediate, cylindrical-form body or neck of uniform size. The entire length of a spermatozoön is about $\frac{1}{800}$ inch. When freshly ejected with the spermatic fluid spermatozoa exhibit active, eel-like movements, as though endowed with separate life, and under favorable circumstances—warmth and moisture—they long retain this capability. These movements may be observed in the body for several days after death, and in the uterine secretion longer than a week. The cause of the movements in spermatozoa is unknown, though it has been contended that they are mere floating cilia. Acid liquids stop these movements immediately, as do strong alkalies, especially ammoniacal liquids; also distilled water, alcohol, ether, etc. Spermatozoa show great resistance to chemical reagents. They do not dissolve completely in sulphuric acid, nitric acid, acetic acid, nor in boiling-hot sodium solutions; but they are dissolved in boiling caustic-potassium solution. They resist putrefaction, and after drying they may be obtained again in their original form by moistening them with a 1-per-cent. sodium-chloride solution. By careful heating and burning to ash the shape of these bodies are said to be seen in the ash (Hammarsten).

As found in the urine spermatozoa are nearly always in the quiescent state, and they may be found in the urine which has stood for days, their typical form being well preserved (Fig. 29).

Clinical Significance.—Spermatozoa are only found in semen or fluids mingled therewith. Their persistent absence from seminal fluid indicates sterility or incapability of procreation.

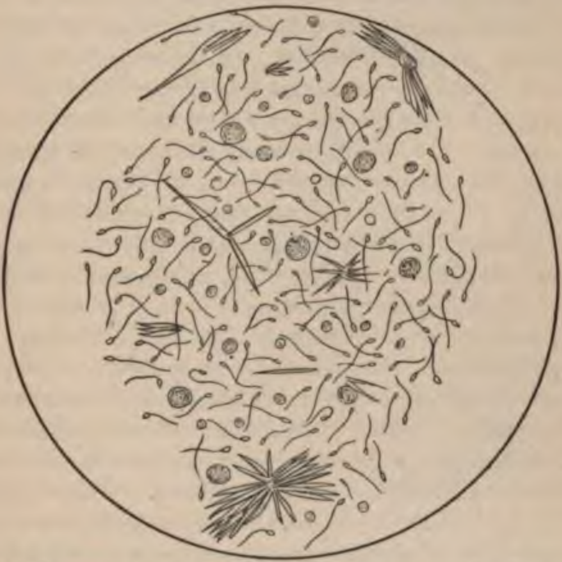

FIG. 29.—SPERMATOZOA IN URINARY SEDIMENT. (After Peyer.)

Spermatozoa may be found in the urine after every ejaculation of seminal fluid, and therefore they may aid the physician in detecting masturbation. Spermatozoa are found in the urine in some cases of severe illness, such as typhoid fever, typhus pneumonia, and after epileptic attacks. A very constant deposit of spermatozoids in the urine constitutes an essential feature of spermatorrhœa. In such cases the urine often shows the presence of white flakes, which under the microscope appear as masses of spermatozoa and finely-granular matter.

FRAGMENTS OF TUMORS.

Contrary perhaps to general belief, fragments of new growths are rarely met with in the urine, and those that are occasionally encountered nearly always originate in the bladder. Small polypi have been found in the urine a few times, as well as fragments of villous growths. More often, perhaps, carcinoma of the bladder parts with some of its constituents, which subsequently appear in the urine. In such cases the fragments are usually necrotic, and therefore practically impossible to recognize. The typical villous growth appears in its finest subdivisions as characteristic, tree-like branches—"*fringe-like*"—which consist of enlarged vessels covered with a single layer of epithelium; but, owing to the necrotic changes resulting in their disintegration, these fragments are seldom seen in the urine in typical form. The epithelium has usually undergone molecular degeneration, accompanied by bacterial life, and the villus itself is infiltrated with the products of suppuration. It is only occasionally that forms are met with which assist in diagnosticating villous growths. Thus, crystals of hæmatoidin may be observed in the necrotic masses, or they may be brought out frequently by treating the masses with glycerin. They may be recognized by their brownish-yellow color; small, rhomboidal form; or yellow, grass-like tufts. Treated with nitric acid and observed under the microscope, the well-known play of rainbow colors reveals the presence of biliary coloring matters. Since hæmatoidin occurs in the urine only in isolated crystals, it follows that, if found imbedded in necrotic masses, it goes far to establish a diagnosis of cancer, since such conditions are only found with such growths (Jaksch). Hæmatoidin villus is rarely recognized save in acid urine, because in alkaline urine the villous tissue is more disintegrated and mixed with phosphatic deposits.

Cancer of the kidney can rarely, if ever, be diagnosticated from the nature of the anatomical sediments in the urine. The transitional epithelium, more or less abundantly present in all inflammatory conditions of the urinary tract, simulates so closely those of cancer that it is never safe to draw any positive conclusions as to the presence of cancer from this source. It is only when considered in connection with other symptoms, such as hæmorrhage, pain, cachexia, etc., that a positive diagnosis may usually be reached.

BACTERIURIA.

It has been generally accepted that healthy urine when freshly voided is free from bacteria, and is, in fact, an aseptic fluid. Over thirty years ago Pasteur demonstrated that such urine is sterile, and this has been repeatedly confirmed since. If, however, the ordinary normal urine be allowed to stand for some time at ordinary temperatures it becomes crowded with micro-organisms. This is due to the fact that the urine contains so large a percentage of organic matter that it practically constitutes a culture medium for many forms of these organisms.

Abnormal urine nearly always contains micro-organisms, of which nearly forty varieties have been isolated to date. They practically all belong to the class of fungi, and for purposes of study may be divided into two classes, viz.: (*a*) *non-pathogenic fungi*, or those which are innocuous, and (*b*) *pathogenic fungi*, or those possessed of pyogenic powers.

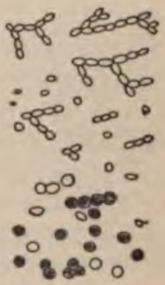

FIG. 30.—YEAST-FUNGUS IN URINE. (After Harley.)

Non-pathogenic Fungi.—These include *molds*, *yeasts*, and *fission-fungi*.

Molds are of comparatively rare occurrence in urine, even when undergoing ordinary decomposition; but if diabetic urine be allowed to undergo alcoholic fermentation, at its conclusion molds make their appearance in quantities upon the surface of the urine, which also becomes crowded with yeast-fungi.

The yeast-plants of the urine (*saccharomyces urinæ*) are single cells of about the size of blood-corpuscles. They are distinguishable from blood-cells by the irregular and occasionally large size of the cells, the presence of a nucleus in the larger sporules, and their more elongated or oval form. Usually these cells are arranged in bead-like forms, some of the beads having several small bud-like cells attached to them (Fig. 30). For their development it is necessary that the urine be distinctly acid, and they cease to multiply if the urine become alkaline. The presence of yeast-fungi in the urine in large numbers may be taken as certain evidence of the presence of sugar.

Fission-fungi are associated with urine tending toward putrefactive changes. Such urine is more or less cloudy when voided; it is never sharply acid; on the contrary, it is usually neutral in reaction or feebly alkaline. Examined under the microscope it is seen to be crowded with micro-organisms in active motion, such as the more common forms in decomposing organic fluids, the most familiar being the well-known *bacterium termo*. The urine on standing does not clear, and, moreover, it does not clear by filtration, and it tends to rapidly pass on into ammoniacal decomposition. This condition of urine is most often met with in weakly and enfeebled people, and in men who have urethral stricture, or who have frequently had catheters or bougies passed. In the process of ammoniacal fermentation of the urine, urea is transformnd into ammonium carbonate through the agency of bacterial life. To each molecule of urea two molecules of water are supplied, and the chemico-vital change wrought by bacterial activity results in two molecules of ammonium carbonate. The chief agent concerned was formerly believed to be the *micrococcus ureæ*, as almost pure cultures of this organism are often observable upon the surface of the decomposing urine. It has recently been shown, however, that nearly all microbes found in the urine possess the above powers to a greater or less extent. The micrococci ureæ are organisms of comparatively large size, and are most frequently observed in long, chain-like strings; although they also occur as free and independent, minute, round objects (Fig. 31).

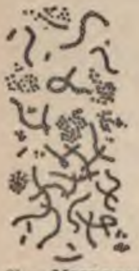

FIG. 31.—MICROCOCCUS UREÆ. (After v. Jaksch.)

Ammoniacal bacteriuria is most frequently met with in cases of obstructive cystitis, in which more or less residual urine remains in the bladder, as often results from paraplegia or enlarged prostate, and urethral stricture of small calibre. The frequent use of instruments in the urethra and bladder often results in this condition.

In addition to the micrococcus ureæ, the urine may contain various other forms of non-pathogenic fungi, including rod-like bacteria of various forms and sizes. Occasionally long, spiral bacilli, with large spores and cocci, are met with in the urine. These are often grouped in various-shaped masses, usually of dark color and variable sizes. For the most part, these organisms gain access to the bladder through the urethra. This may take place through discharges or, more commonly, by the use of instruments.

Pathogenic Fungi.—The pathogenic bacteria found in the urine for the most part belong to two orders,—viz., *micrococci* and *bacilli.*

The *micrococci* found are those characteristic of suppurative diseases in general, and include the *staphylococcus pyogenes albus, aureus, citreus,* and the *streptococcus pyogenes.* The action of these germs is general, which accounts for their frequent presence in the urine. To these must be added the *gonococcus* of Neisser, which will be considered later.

The *bacilli* met with in the urine include the *urobacillus liquefaciens septicus,* the *bacillus coli communis,* the *tubercle bacillus* of Koch, besides a number of others less well known.

In all infective diseases in the healthy organism, if life be not destroyed thereby, the microbes must either be destroyed in the blood and tissues by the process termed *phagocytosis,* or be eliminated through the excretory organs, usually in an active state. The fact of the rapid disappearance of most micro-organisms from the blood, when injected into the circulation of the healthy organism, indicates that the corpuscular elements of the blood have the power of destroying these organisms,—at least, to a large extent. Passing from the blood into the tissues, these organisms meet with the same warfare in the tissue-cells. Should, however, both of these sources of *phagocytosis* prove unsuccessful in destroying these organisms, there still remains a method by which the unassisted organism may rid itself of these microbes,—viz., by means of elimination through the excretory channels; and in this process the kidneys and intestinal canal are the chief organs concerned. The frequency with which the kidneys become infected in the course of general tuberculosis furnishes proof that these organs are the source of elimination of tubercle bacilli. Furthermore, Philipowicz has succeeded in producing tuberculosis in animals by injecting urine into the peritoneal cavity which was taken from tuberculous subjects.

Neumann has demonstrated the characteristic microbes of typhus, pneumonia, and pyæmia in the urine in the course of these diseases, and he has cultivated from the urine, in acute endocarditis and osteomyelitis, the *staphylococcus pyogenes aureus.* Neumann furthermore claims that the microbes which gain access to the circulation often localize in the capillary vessels of the kidney, there causing multiple lesions without involving the whole organ; and through these lesions some of the microbes gain access to the uriniferous tubes and appear in the urine.

Schweiger has conclusively demonstrated that the urine of scarlatinal subjects is distinctly contagious; and he regards all renal lesions arising in the course of infectious fevers of microbic origin. Finally, it may be mentioned that Rimann has conclusively demonstrated the passage of bacilli through the kidneys in the following manner: The bacilli discovered in the pus of ozæna was cultivated in gelatin and agar and stained intensely green; after dilution with physiological solution of salt, the culture was injected directly into the circulation of a dog, cat, and rabbit; after a time these stained microbes appeared in the urine in large numbers.

Of the various pathogenic micro-organisms found in the urine, the recognition of the *bacillus tuberculosis* of recent years claims the greatest clinical interest. It may be stated that the presence of this bacillus in the urine, especially when arranged in **S**-shaped aggregations, or in colonies of irregular masses, points with unmistakable certainty to tubercular ulceration of the urinary tract. Fortunately for diagnostic purposes, if the *tubercle bacillus* appear in the urine at all, it usually occurs in abundance, and may, with recent methods, be recognized in masses often arranged as in pure cultures.

In all cases of purulent urine accompanied by anæmia, wasting, and evening temperature, the urinary sediment should be examined for the presence of tubercle bacilli. Of course, more (*a*) The difficulty often encountered in getting casts to settle in urines of high specific gravity, because renal casts are of comparatively light weight and often float in such urines for hours without subsiding. (*b*) The changes in the urine upon standing often altered the essential features of the deposit, as before stated, sometimes rendering them unrecognizable. (*c*) In urine which stood long enough to secure the sediment, the microscopical field sometimes became so crowded with micro-organisms that the organic products were completely obscured from vision. Happily, these difficulties are now matters of the past; and it is only necessary to secure a freshly-voided sample of urine, submit it to the centrifugal apparatus for two or three minutes, and we have a true and unaltered sediment, that exactly represents the pathology of the urine as it leaves the urinary tract.

The urinary sediment obtained—always preferably by the centrifuge—is best examined in a shallow cell, upon a glass slide carefully covered with a cover-glass. This is best secured by taking up about 4 to 6 drops of the sediment in a nipple-pipette from the bottom of the sediment-tubes of the apparatus, and placing them upon a carefully-cleaned slide, then placing the cover-glass over the cell, and with the thin, freshly-torn edge of a piece of blotting-paper removing the excess of urine, which tends to spread over the cell and along the slide. By this means the sediment constitutes a temporary mount, so that it may be examined at any angle without flowing out of the cell. The slide is next placed under the microscope, which is adjusted with a $\frac{1}{4}$-inch objective for ordinary search, and examination conducted in a clear, but not too bright, light.

The greatest difficulties encountered in searching for casts in the urine will usually be met with in the case of narrow hyaline casts. These bodies are so transparent and non-refracting that they are exceedingly liable to be overlooked. This may often be avoided by proceeding as follows: After securing an accurate focus of the field by careful regulation of the fine adjustment of the instrument, gradually darken the field by the mirror-adjustment and throw the light obliquely across it, illuminating the field, in fact, but about one-half or two-thirds its extent. Next, by slowly moving the slide about, the different features of the

patient search is necessary than in the examination of sputa, owing to the dilution of tubercular pus by the urine, and it is necessary to concentrate it as much as possible for the same reasons. This is best accomplished by the centrifuge for obvious reasons. The purulent deposit of tubercular urine should be treated precisely as the sputum in searching for tubercle bacilli. Should difficulties be encountered in finding the bacilli when the symptoms strongly point to their presence, or should doubts arise as to the true character of the bacilli found in the urine in any given case, the inoculation of animals with the sediment or plate cultures thereof should be resorted to before negative conclusions can be positively reached. Indeed, unless the time required for the latter be a matter of importance in the case (which is very seldom), the plate cultures are the easiest and most certain method of success.

Gonococci were first discovered in the pus of gonorrhœa by Neisser. They consist of minute, roll-shaped cocci. They are chiefly met with as diplococci, the individual cocci being seemingly divided by a bright, transverse band, often presenting the so-called "*roll-form*"; also termed "*kidney-*" or "*bean-*" *shape.* The cocci usually appear in pairs lying close together, their flattened surfaces usually presented to each other. They multiply by each coccus splitting in two. Bodies in all respects resembling gonococci, so far as present methods are able to determine, have been found in the genital tract under the most variable conditions, and this fact has tended greatly to diminish the diagnostic value of these organisms. On the other hand, it is pretty well established that the presence of gonococci within pus-cells in purulent urethritis is characteristic of infective gonorrhœa. In all cases of recent infection with gonorrhœa the specific gonococci are to be found within the pus-cells in abundance, although they are not limited to this location, but may be seen in the epithelia, as well as floating in the liquor puris. This cannot be said of the non-infective forms of diplococci. The gonococcus is best stained in gentian violet, methylene blue, or fuchsin, after which it may be rinsed in water and examined under the microscope.

VERMES.

Distoma Hæmatobium.—This parasite has frequently been found in the portal vein and its branches, in the splenic and mesenteric veins, and in the venous plexuses of the bladder and rectum (Fig. 33). From the investigations of Bilharz, it would seem that more than half the adult Fellaheen and Coptic population of Egypt suffer from this parasite.

The eggs of this parasite are found in numbers in the urinary passages and in the urine. They are usually accompanied by blood, pus, and sometimes by considerable fat. The eggs are oval, flask-shaped bodies, with rather sharp projections from their anterior extremities. They measure rather less than $\frac{1}{200}$ inch in length.

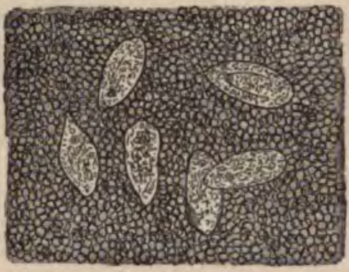

FIG. 32.—EGGS OF DISTOMA FROM URINARY SEDIMENT.

When confined to the larger veins, these parasites do not produce much damage; but if they invade the smaller vessels, notably those of the submucous tissues of the urinary tract, they induce severe and, in some cases, fatal consequences. In the intestines the result is often that of severe dysentery.

The most serious results of the ravages of this parasite are met with in the urinary passages. The lesions produced here, according to Griesinger, consist of raised patches of injected and ecchymosed tissue, which often pass into ulcerations, giving rise to severe hæmorrhages. These patches are covered with mucus and brownish exudations of bloody matters containing masses of ova. If no lesions of the mucous membrane occur over these patches, they may remain as nodules of more or less firm and indurated tissue.

When these parasites invade the ureters and renal pelvis, the results are apt to be still more serious, as they threaten the integrity of the kidney from two sources. First, by consequent thickening they may cause occlusion of the ureters and resulting hydronephrosis or pyonephrosis, as in a case observed by Griesinger. Second, severe pyelitis is often set up by invasion of the renal pelvis, which may result in ascending pyelonephritis.

In addition to these consequences the masses of ova extruded into the urinary passages are exceedingly liable to become the nuclei for urinary calculous formation; and, indeed, this is claimed to constitute the cause of the great frequency of calculous disease in Egypt.

From the variety of lesions caused by invasion of the *Distoma* *hæmatobium*, as might be expected, a corresponding variety of clinical symptoms result. In the milder cases but little disturbance of the urinary function is to be observed. Some pain, described as of a burning character, is notable on micturition. This, however, is but momentary, and is chiefly due to the passage of the ova along the urethra, which they irritate by means of their sharp projections. At the termination of micturition a few drops of blood, or a blood-clot, are sometimes noted. The urine contains pus and blood-cells, with the eggs of the parasite as represented in Fig. 32. The symptoms become more distressing with the involvement of the bladder, entailing various grades of cystitis, always accompanied by more or less hæmaturia. To these may be added the discomforts and deterioration of the general health entailed by pyelitis when the parasite invades the renal pelvis. Septic infection, nephritis, and uræmia are among the most serious consequences entailed by extension

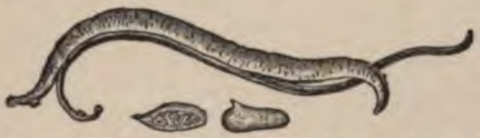

FIG. 33.—DISTOMA HÆMATOBIUM, MALE AND FEMALE, WITH EGGS.

of the morbid changes set up by the parasite in the upper urinary tract. Finally, it may be noted that Bilharz and Griesinger, during the course of their investigations in Egypt, found strong evidence that the distoma disease sometimes takes the course of an acute and rapidly fatal disorder. Griesenger observes: "We found on two occasions, in the bodies of persons who had rapidly died from an unknown acute disease, abundant recent distoma changes in the bladder, recent pyelitis, and a uniform dark-red hyperæmia of the kidneys. In other cases of supposed rapid typhus the same changes were found in the bladder and ureters."

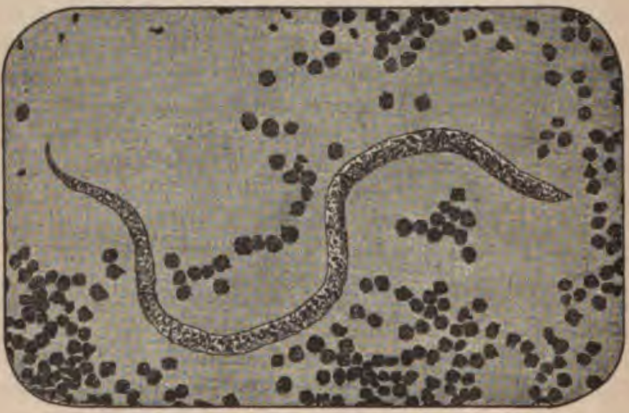

FIG. 34.—FILARIA IN HUMAN BLOOD. (After Mackenzie.)

Filaria Sanguinis Hominis.—Dr. Lewis, of Calcutta, was the first to describe this parasite as occurring in the human organism. In 1872 Lewis made the interesting announcement that, as observed in India, chylous urine always contained large numbers of these parasites. He later on discovered that these worms were present in great numbers in the blood of patients suffering from chyluria. This hæmatozoön is about the width of a red blood-corpuscle and about fifty times longer than its width. It possesses a short, rounded head, with a tongue-like protuberance, and a rather long and pointed tail. The parasite is inclosed in a loose sac, in which it moves with freedom. This covering appears structureless, but the parasite itself, as viewed under the microscope, is seen to be very granular, with transverse striations.

It was early supposed that the minute hæmatozoön described and figured (Fig. 34) was but the young of a larger, parent worm, and in 1876 Bancroft, of Brisbane, succeeded in demonstrating the mature worm in a lymphatic abscess of the arm. The mature form is a nemotode worm, about the thickness of a hair and three or four inches in length. Dr. Mason has established the origin of this parasite in the mosquito, which deposits the larva in ponds, the water of which being swallowed, the subject becomes the seat of its further development. The most curious and interesting circumstance in reference to the habits of this parasite is the fact, pointed out by Mason, that the embryo filaria is very active at night, but quiescent during the day; it is therefore to be found abundantly in the blood of subjects of this disease during the night, but not to be found during the day. Dr. Mackenzie observed, however, that upon reversing the order of sleeping and waking, the filariæ changed their nocturnal habits,—coming out when the subject slept and remaining hidden during the waking hours. It would, therefore, seem that the activity of filariæ in the blood depends upon quiescence of the subject. What becomes of the filariæ, or where they conceal themselves temporarily during their disappearance, as yet remains a mystery.

The filariæ, though greatly obstructing the lymph-channels and literally swarming in the blood, of themselves do but comparatively little mischief. The embryos appear to pass readily through the capillary vessels without causing obstruction, irritation, or emboli. It is, however, altogether different with the ova if they remain unhatched in the blood, lymphatics, and the urine. Owing to their greater diameters, they become arrested in the smaller lymphatic vessels and, becoming impacted, accumulate until the gland becomes impervious, resulting in lymphatic congestion and even necrotic changes; *elephantiasis*, or *lymph-scrotum*, is one of the results of this condition. Chyluria is one of the most frequent consequences, also, of this condition. This is brought about through the obstruction of the larger lymphatics, the thoracic duct, or large channels between it and the urinary organs.

Echinococci.—The hooklets and scolices of the echinococcus cyst are among the rarer forms of sediments met with in the urine (Fig. 35). It is exceptional for echinococci cysts to develop in the urinary passages; more often the products of these cysts make their way into the urinary passages from the kidney or some neighboring organ by means of rupture. If the characteristic hooklets appear in the urine, they are usually accompanied by blood, pus, and more or less cellular *débris*, as well as shreds of the membrane forming the cystic envelope.

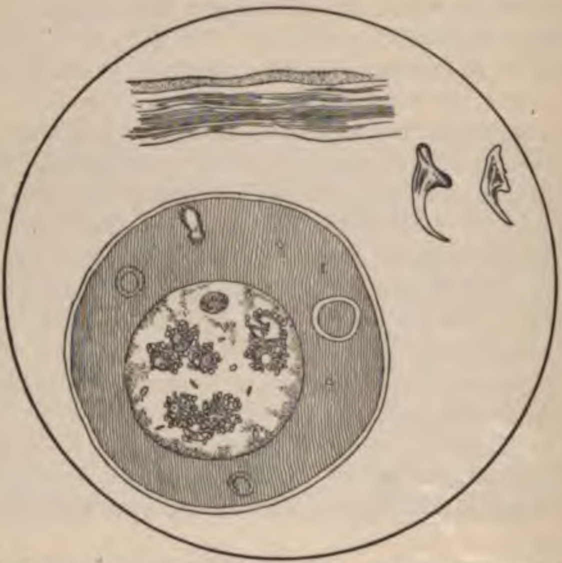

FIG. 35.—ECHINOCOCCUS, WITH TWO HOOKLETS AND SECTION OF CYSTIC MEMBRANE GREATLY MAGNIFIED. (After Peyer.)

Echinococci are minute ovoid parasites barely visible to the naked eye. They consist of a head not unlike that of the tapeworm, provided with four mouths or suckers and a double row of hooks. The echinococci are developed within a germinal membrane, and exist in groups of from six to ten. The hydatid growth consists of an outer, fibrous capsule by which it is attached to the organ in which it is developed. Within the capsule is the hydated cyst, which varies in size from that of a marble to that of a distended urinary bladder, or even larger. Within the large cyst a great number of secondary or so-called *daughter-cysts* develop and float freely in a serous or rather saline, aqueous fluid. These *daughter-cysts* also vary in size from that of an apple to minute points requiring the microscope for their recognition. The *mother-cyst* may, in rare cases, be entirely barren,—*i.e.*, contain nothing but fluid,—or it may contain thousands of secondary or *daughter-cysts.*

Siebold pointed out the interesting fact that the hydatid worm in man is the encysted form of development of a very minute tape-worm which infests several animals, notably the dog, pig, monkey, sheep, etc. This tape-worm is the *Tænia echinococcus*, and is very minute—about the size of a millet-seed. The intestines of the dog are usually infested with great numbers of these worms. The eggs are discharged with the stools, and, finding their way into food, reach the stomach in man, where they find suitable conditions for their development. The embryo, upon hatching in the stomach, burrows its way or is carried by the blood to some organ,—most often the liver or kidneys,—where it develops as the hydatid vesicle, in which are contained the echinococci described. In Iceland, where the natives live with their dogs in huts, it is said that one-seventh of the deaths are due to the ravages of these parasites.

Strongylus Gigas.—This nematode worm has been found in the renal pelvis of dogs, wolves, horses, oxen, and other animals, and less frequently in the human kidney. It somewhat resembles the *Ascaris lumbricoides*, but it has six papillæ about the mouth instead of three, and it attains a much greater length,—one to three feet,—and it is nearly a quarter of an inch in thickness. It may further be distinguished from the common round intestinal worm by its reddish color. This parasite may be said to be peculiar to the kidney, being very rarely met with elsewhere. Leuckart has, after some research, questioned the appearance of this parasite in the human organism, but there is, beyond doubt, at least half a dozen well-authenticated cases on record, in addition to a specimen in the Hunterian Museum, taken from the kidney of a patient of Sheldon's (Dickinson).

In addition to the parasites described, *ascarides* have been found in the urine in exceptional cases. In such cases the worms have usually made their way from the lower intestines into the urinary tract, usually by way of abnormal openings. In cases of women, these thread-worms have made their way into the bladder through the urethra.

SECTION VIII.

GRAVEL AND CALCULUS.

CONCRETIONS of a more or less hard and dense character are liable to form in the urinary passages. These bodies are variously termed, according to their size, location, etc., *sand*, *gravel*, *stone*, and *calculi*. These formations are called *primary* when they are deposited from urine which has undergone no decompositional changes, and are the result of some original defect of, or foreign addition to, the composition of the urine. The *secondary* formations, on the other hand, are due to decomposition of the urine with resulting precipitation of its elements, and, for the most part, comprises those ammoniacal changes of the urine resulting from inflammatory disorders of the lower urinary passages. Concretions of small size—not too large to make their way spontaneously through the urethra—have been somewhat arbitrarily termed gravel; while, on the other hand, the larger concretions have received the name of stones or calculi. Concretions vary greatly in size; some of them being so minute as to require the microscope for their recognition, while others attain the enormous size of an orange or even larger. The smaller concretions mostly emanate from the kidneys or renal pelvis, while those of large size come from the bladder.

The most practical classification of urinary concretions is that which corresponds to the chief constituents of which they are composed. This comprises the following divisions: (1) *uric acid;* (2) *urates;* (3) *oxalate of lime;* (4) *cystin;* (5) *xanthin;* (6) *urostealith;* (7) *basic calcium phosphate;* (8) *calcium carbonate;* (9) *calcium phosphate with ammonio-magnesium phosphate.* These are all strictly of urinary origin, and composed of urinary ingredients. In addition to these, at least two other classes of concretions are met with, whose origin are extra-urinary, viz., *prostatic calculi* and *fibrin* or *blood concretions.*

Concretions may consist exclusively of one ingredient, uric acid and calcium oxalate being the most frequent examples.

Far more frequently, however, two or more primary deposits occur in separate and alternate layers, constituting the so-called "*alternating*" calculus, the most common of which are those composed of uric acid and calcium oxalate. The number and thickness of these layers in alternating calculi vary very greatly according to the age of the calculi and the frequency of the changes giving rise to the alternating deposits. The thickness of the layers also varies to some extent inversely with their number.

If a calculus consist of but one primary substance, its arrangement is usually stratified, exhibiting a larger or smaller number of concentric layers. Such are usually uric-acid, calcium-oxalate, and phosphatic formations. The great majority of concretions consist of a central division or *nucleus*, and an excentric division or *body*. There may be in addition, especially in old or large calculi, an external envelope or *crust*, which is nearly always phosphatic. The nucleus varies much in size and composition. It may consist of the same material as the body of the calculus, especially when the latter is made up of such primary deposits as uric acid, calcium oxalate, etc. Frequently, however, the nucleus consists of some organic product, as blood-clots, coagulated mucus, or epithelium. Exceptionally foreign bodies introduced from without into the bladder become the nuclei for subsequent calculous formations.

The causes of urinary concretions comprise (*a*) the conditions favorable for their origination; (*b*) the conditions favoring their formation and growth. The conditions favoring the origin of calculi have received some light through the researches of Carter, who found that the actual nucleus nearly always consists of globular forms of urates and calcium oxalate, rather than crystals of these substances; and, furthermore, that a colloid matrix was always an essential element of the nuclear formation. Rainey and Ord have furthermore shown that the globular forms of urates and oxalates referred to are only produced when precipitation occurs slowly in the presence of a colloid medium. From this it would appear that morbid conditions of the urinary passages accompanied by exudations of colloid matter, such as mucus or albuminoids, constitute the initial step in the formation of calculi. In the presence of such colloids precipitation of urates, oxalates, etc., occurs, which, combining with the colloids, form globular aggregations that constitute the basis for subsequent development of stone. The conditions favoring the growth and development of concretions embrace chiefly the states of the system or of the urine itself which favor precipitation of the urinary solids. Under the first set of causes may be mentioned digestive disorders, organic diseases of the kidneys, and diseases of the urinary passages, most notably cystitis. The conditions of the urine favoring the growth of calculi are variable, and in some cases directly opposite. Among these causes may be mentioned (*a*) excess in the urine of the precipitated substance; (*b*) overacidity of the urine. This disposes more especially to the growth of uratic concretions, as it diminishes the solvent powers of the urine over uric acid and the urates, thus leading to their precipitation. (*c*) An alkaline condition of the urine. This may lead to precipitation of the phosphates or carbonates of calcium and magnesium. If the urine be alkaline from fixed alkali, the earthy phosphates or carbonates of calcium may be precipitated and favor calculous growth of that order,—a rare condition, however. If the urine be alkaline from volatile alkali—ammonium—the result is precipitation of triple-phosphate of ammonium and magnesium,—an exceedingly common occurrence. (*d*) Deficiency of urinary salines and of sodium and alkaline phosphates in the urine weaken its solvent powers over the urates and cause precipitation. (*e*) Lastly, deficiency of the normal urinary coloring matters greatly weakens its solvent powers and favors precipitation of various constituents, especially uric acid and the urates.

URIC-ACID CONCRETIONS.

Calculi composed entirely or chiefly of uric acid comprise the great majority of stones met with in human urine. Statistics give the proportion to all other forms at from 75 to 90 per cent. Indeed, the great frequency of this form of gravel led early observers to the conclusion that all stones were composed of uric acid in whole or in part; hence the name lithuria, for a long time, was applied to gravel in general, and even at the present time is sometimes erroneously applied.

Uric acid may be passed in the form of crystalline clusters, or as smooth, spherical bodies, ranging in size from a pin-point to that of a grain of wheat, or, again, in roughened concretions as large as a pea. These are derived from the kidney or renal pelvis, and may be washed out with the urine singly or in numbers at different intervals. The passage of uric-acid gravel from the kidneys is usually attended by more or less pain, sometimes, indeed, so acute that it has received the name of "*renal colic.*" All these uric-acid concretions present a yellowish-brown or reddish appearance. If retained in the bladder, these small concretions grow, more or less rapidly, into round or oval or elongated and flattened stones. Their surfaces are tuberculated and irregular, and they vary in weight from a few grains to four or five ounces. They are hard and brittle, and, upon section, they may be seen to be marked with concentric laminæ.

Uric acid may be recognized by the murexid test (see page 33). It is soluble in solutions of lithium, potassium, and sodium, and also in piperazin, while in solutions of sodium and potassium bicarbonate it is insoluble, as well as in water and dilute acids. Since the combination of uric acid and lithium is more soluble in water than its combination with sodium or potassium, it has become popular to treat the so-called uric-acid diathesis with mineral waters containing a few grains of lithium carbonate to the gallon. As Bunge has shown,[1] however, "this *naïve* idea simply implies ignorance of Bertholett's law in reference to the diffusion of bases in the economy, as no such solvent action of uric acid in the economy is obtained thereby."

The formation of uric-acid calculi is most frequent in early and late life; that is to say, in children and old people. A highly-acid state of the urine is the most essential condition for deposition of this form of concretion. Uric acid frequently forms the basis of calculi which, subsequently, becomes the nuclei for further formation with other urinary constituents, constituting mixed calculi. The most frequent of these secondary formations is calcium phosphate; less frequently, calcium oxalate. Should the urine become alkaline at any time from volatile alkali, triple phosphates will be deposited and add to the growth of the calculus. This, indeed, is almost an essential in the late stages of calculous life in the bladder, since alkaline urine is one of the features of vesical inflammation which attends nearly all calculi of any size, especially during their late sojourn in the bladder. The conditions favoring the deposition of uric acid have been more fully considered in another section of this volume (page 32).

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[1] Text-Book of Physiological and Pathological Chemistry, London, 1890, pp. 356 and 357.

URATE CONCRETIONS.

Urates rarely constitute the sole constituent of stone in adults, but with uric acid they are frequently met with in the calculi occurring in children. On the other hand, in connection with calcium oxalate, urates form a large percentage of calculi found. Urate concretions have been regarded as consisting of ammonium urate, but calcium and sodium are to be found in them quite generally upon analysis. They do not attain a large size, as in the case of uric-acid stones, rarely being found larger than a small marble. They are usually of a light-grayish color and multiple in number, two or more being found together. They are not so hard and dense as the uric-acid calculi. Like uric acid, urate stones are nearly always deposited from acid urines; the exceptions to this rule consist chiefly of the mixed stones of triple phosphate and ammonium urate, which are the outgrowths of ammoniacal urine.

The urate deposits possess a great tendency to form infarcts in the renal tubules during early infancy. These consist of ammonium and sodium urate, which form yellowish-brown lines, often reaching from the papillæ to the bases of the pyramids, following the lines of and blocking the interiors of the large, straight, uriniferous tubes. They occur most frequently from the second to the tenth day after birth, although they may occur as late as ten or twelve weeks after birth. It is significant that these infarcts are not found in the kidneys of stillborn children. The conditions leading to these deposits in infants is physiological rather than pathological,—due to the highly-concentrated state of the urine at birth; the deficiency of aqueous elements in the urine does not permit either of solution or washing out of the uratic components of the urine, which, upon the establishment of respiration, become greatly in excess.

In febrile conditions in children deposits of sodium urate are common, and no doubt frequently form the nuclei and primary deposit for the subsequent development of gravel. The frequent occurrence of calculi in children may be largely attributed to this source.

CALCIUM-OXALATE CONCRETIONS.

Oxalate-of-lime concretions are met with most often as large, rough, dark, tuberculated masses commonly called "*mulberry calculus.*" Less often they occur as small, rounded, smooth, dark-grayish bodies, called "*hemp-seed*" calculi. Calcium-oxalate concretions are extremely hard and brittle, and when crushed present sharp, angular lines of fracture. The nucleus often consists of uric acid or urates, or it may be colloid. Pure calcium-oxalate calculi are often met with, but much more frequently mixed calculi of calcium oxalate and uric acid occur in alternating strata around a mixed nucleus. Less often calculi are met with consisting of oxalate of lime as the basis, surrounded by a more or less deep incrustation of triple phosphate.

The urine associated with calcium-oxalate calculi is always acid, unless in cases of long standing, in which the stone has set up cystitis, when it may be found ammoniacal. In short, the condition of the urine in these cases is very similar to that with uric acid, as might be expected from the fact that calculi are so often encountered composed of alternating layers of these two substances.

CYSTIN CALCULUS.

This form of concretion is comparatively rarely met with in practice. Although not usually attaining the large size of uric-acid calculi, they may be found in the bladder exceptionally of considerable dimensions. As a rule they are of medium size, oval or cylindrical in form, with finely-granular surfaces, over which may be seen small crystals of a decidedly yellow color. Although these concretions are rather soft and compressible, they break with a crystalline fracture. Upon section they present a radiated appearance of yellow color not unlike bees-wax, but they turn gray upon exposure to light. The causes of cystin deposits in the urine have already been discussed in the preceding section. The most notable feature in this connection is its tendency to occur repeatedly in members of the same family. Cystin is readily recognized by its ready solubility in ammonium, depositing, upon evaporation, its beautiful and characteristic six-sided crystals. It is also soluble in mineral acids as well as in the fixed alkalies and their carbonates; while it is precipitated by vegetable acids and ammonium carbonate.

XANTHIN CONCRETIONS.

Xanthin calculi are exceedingly infrequent; in fact, they are perhaps the rarest of all concretions met with in the urine.[1] They seem to be entirely confined to young subjects, none as yet having been met with either in adult or in advanced life.

Xanthin concretions are of a whitish, yellowish-brown, or cinnamon-brown color, of medium hardness, with amorphous fracture, and on rubbing appear like wax. They vary in size from a pea to that of a hen's egg. They burn completely when heated on platinum-foil. They give the xanthin reaction with nitric acid and alkali, which should not be mistaken, however, for the murexid reaction.

CALCIUM-PHOSPHATE CONCRETIONS.

Phosphate-of-lime calculi are among the rarer forms of unmixed concretions. They possess a chalk-like appearance and break with an amorphous fracture. They may be dense in structure or loose and spongy. Two forms of calcium-phosphate calculi occur: (*a*) Round or oval-form, varying in size from a small bean to a hen's egg. These are of a white, chalky appearance, of friable surface, and break with an amorphous fracture. These are usually vesical calculi of elderly people, especially dyspeptic people with alkaline urine. (*b*) The second form are irregular, sometimes branched in shape, of a grayish-white color, compact in texture, brittle, and of porcelain-like fracture. These are usually found in cysts and pockets of the urinary channels, and appear to be of local origin.

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[1] Less than a dozen cases are at present on record.

The earthy phosphates are often abundantly deposited in the urine, but, owing to their amorphous form, they possess little tendency to concrete; otherwise this form of calculus would doubtless rank among the most frequent of urinary concretions. It is well known that patients may void alkaline urine, turbid from undissolved earthy phosphates, for months without stone formation.

AMMONIO-MAGNESIUM-PHOSPHATE CONCRETIONS.

Calculi composed exclusively of this salt are uncommon; but, on the other hand, it very frequently forms the exterior of other forms of calculi, such as uric acid or calcium oxalate. Ammonio-magnesium-phosphate concretions are always significant of ammoniacal urine, and herein lies the explanation of its frequency as a secondary deposit upon other primary concretions. The mechanical irritation set up by any primary calculus of much size invariably leads to ammoniacal decomposition of the urine, usually in the bladder. The result of these changes is prompt precipitation of triple phosphates of highly-crystalline nature, and therefore readily tending to concrete upon any nucleus in the bladder. It has been stated that triple phosphate calculi are rare; this applies to concretions of marked size.

MIXED PHOSPHATE CONCRETIONS.

The most common variety of mixed phosphatic calculi are those composed of calcium phosphate with triple phosphate of ammonium and magnesium. This has been termed the "fusible calculus," because under the blow-pipe it fuses into a black, enamel-like mass. These calculi often attain a large size. They are of grayish-white color, often covered on the surface with bright, glistening points,—triple phosphatic crystals. In texture they are friable and somewhat spongy, often composed of concentric strata, easily fractured into thin laminæ, the fractured surfaces often presenting bright deposits of crystalline triple phosphates. This calculus is very soluble in mineral acids, but is insoluble in water and alkalies; its chief characteristic is its fusible property under the blow-pipe.

These calculi nearly always form upon some other primary nucleus, such as uric acid or calcium oxalate, and they often incrust fungous or other growths of the bladder. They are always the result of ammoniacal urine. and originate chiefly within the bladder.

CALCIUM-CARBONATE CONCRETIONS.

Concretions of carbonate of lime belong to the rarer forms of calculi met with in human urine, very few authenticated cases being on record. They are small in size, of smooth surface, gray or bronze-like in color, and often very hard in texture. They are mostly spherical in shape, often translucent, and on section present numerous concentric lines. The nucleus is usually multiple, and upon crushing these calculi they break into sharp fragments.

OTHER FORMS OF CONCRETIONS.

A few additional varieties of concretions are occasionally met with in the urine.

Fatty Concretions.—These consist of fatty matters saponified by the alkalies of the urine. This substance has received the name of *urostealith*. These concretions are soft and friable, usually of brownish or yellowish color, and often incrusted with phosphates. They burn with a flame when heated on platinum-foil, and give off an odor similar to resin or shellac. These calculi have only been met with a few times.

Indigo Concretions.—Indigo has been met with in the urine in the form of calculus. It is doubtless derived from the indoxyl-potassium sulphate of the urine, which may be changed by highly-acid urine into indigo. Such cases are exceedingly rare, however, but one or two having been recorded.

Fibrin and *blood concretions* are mentioned as having been met with in the urine, but these must be looked upon as anomalous occurrences, except as forming the nucleus of other calculous growths.

Prostatic Concretions.—Prostatic calculi may be mentioned as sometimes encountered in the urine, although not strictly speaking urinary products. Sir Henry Thompson found these calculi invariably in the adult prostate at the autopsy. They are found in the follicles of the prostate; at first consisting entirely of albuminoid matter, they later become impregnated with earthy matter, and ultimately become as hard as other forms of calculi. It is exceptional that they give rise to special symptoms; only so when they attain an unusual size and encroach on the gland-tissue or project into the urethra. It is only exceptionally that these concretions are spontaneously discharged with the urine.

Clinical Differentiation.—It would add greater precision to the treatment of calculus if the nature of the stone could be made out. The accuracy with which this can be compassed will vary considerably in different cases. The most trustworthy information is obtainable from examination of calculi already voided with the urine. In a very considerable percentage of cases the habit of spontaneous expulsion of small concretions has been established. If the discovery of a retained calculus be not too remote from the spontaneous passage of a concretion which has been secured and examined, and, furthermore, if the characters of the urine correspond, it furnishes the most certain evidence of the nature of the retained calculus. It is of the utmost importance, therefore, to preserve all concretions that may be spontaneously voided with the urine, however minute they may be, and to make an accurate note of their composition, as well as of the characters of the urine at the time they were voided.

In the absence of the above information it is still possible, in a large majority of cases, to make out with very great probability the composition of the retained concretion. The evidences here are to be drawn from the characters of the urine—notably its chemical reaction and the character of the deposits. In addition to these, certain inferences are to be drawn from the constitutional peculiarities of the patient, as well as the age, together with the known frequency of the different forms of concretions considered with regard to their location.

If the urine be frankly acid *at the time voided*, the calculus is nearly certain to be either uric acid or calcium oxalate. Uric-acid calculi being by far the more frequent, the chances are in favor of the presence of that form of concretion. If, in addition to the *sharply-acid* reaction of the urine, *directly* upon cooling it precipitates crystals of uric acid, and the symptoms appear in vigorous subjects addicted to the liberal use of meat diet, it becomes reasonably certain that the calculus is of the uric-acid form.

If, on the other hand, the *freshly-voided* acid urine precipitate habitually the calcium-oxalate crystals, the patient being of sedentary habits and prone to indulgence in the use of both saccharine and proteid foods, it may be pretty confidently concluded that a calcium-oxalate calculus is retained. As already observed, calculi are very frequently met with composed of alternating layers of uric acid and calcium oxalate, because they are both the outgrowth of acid urine, as well as largely of similar habits of living. But the predominance of either variety may usually be made out by repeated observation of the features just considered. Cystin and xanthin concretions are also met with in acid urine, but these formations are so rare that they may, for practical purposes, be ignored, unless the presence of these substances be discovered in the urinary sediment, in which cases the probability of the presence of these rarer forms of calculi may become a proper subject for consideration.

The forms of calculi met with in *alkaline urine* next demand attention. For the most part these are vesical calculi. As a rule, they are more complex in composition, because the conditions of the urine during the formation and growth of these concretions are subject to greater change. Renal calculus is frequently composed of a single constituent, because its origin and growth is practically in the same location and subject to the same conditions of the urine throughout. With vesical calculus, on the other hand, the nucleus may originate in the kidney when the urine is acid, or even alkaline from fixed alkali, while its subsequent development occurs in the bladder, where the urine may be ammoniacal, as a consequence of its residence there or otherwise, and its growth will be influenced by the elements consequent to ammoniacal urine.

The most frequent calculus met with in alkaline urine is that composed of mixed phosphates, or the calculus with uric-acid or urate nucleus covered with mixed phosphates. If the urine be alkaline from fixed alkali, the calculus is pretty sure to consist of calcium carbonate or phosphate. In such cases the urine has usually long been alkaline, and the calculus is likely, accordingly, to consist uniformly of the same substance throughout.

If the urine be ammoniacal the nucleus and body of the calculus is very likely to be composed of different substances. The nucleus may be uric acid, urates, or oxalate of lime, but the crust is pretty sure to consist of mixed phosphates. Remembering the rapidity with which urine undergoes ammoniacal changes in vesical disturbances, special care should be observed to see if the urine be ammoniacal in these cases *at the time it was voided*, otherwise the observer may be greatly misled in his conclusions. The intensity of ammoniacal reaction of the urine, the deposit of phosphatic fragments, and the amount of deposit of triple-phosphate crystals, together with the grade of the accompanying cystitis, will furnish some idea of the age and magnitude of the phosphatic calculus.

Analysis of Calculi.

In conducting the analysis of urinary calculi the size, color, form, and density of the concretion should first be noted, as these often indicate, with considerable probability, their composition, or at least the direction in which the chemical examination should be pursued. Since many calculi are composed of more than one deposit, in order to ascertain with greater precision the several components, section should first be made of the calculus by means of a fine saw. If the calculus be brittle it will often answer the purpose to break it into as large pieces as possible. Upon section or fracture, portions should be scraped from the different-appearing strata for separate examination. A portion of the calculus should first be subjected for some time to a red heat upon platinum-foil, either over a spirit-lamp or by means of a blow-pipe. In the latter case the best method is to lay the platinum-foil on a plaster-of-Paris cast, when the powdered calculus and foil may be raised to any desired degree of heat without danger of burning the fingers. If upon ignition little or no fixed residue be left, the calculus is composed of some of the organic deposits—as uric acid, ammonium urate, xanthin, cystin, proteid substances, or urostealith. If, on the other hand, the fused calculus leave a considerable residue, it consists of some of the inorganic bases, either alone or in combination, such as urates of sodium, potassium, or ammonium, calcium oxalate, calcium carbonate, calcium phosphate, or ammonio-magnesium phosphate.

If the concretion burn up and leave little or no residue, it is necessary next to proceed by chemical methods to determine which of the organic deposits it be composed :—

Uric Acid.—A portion of the powdered concretion is submitted to the murexid test (see page 33), and if the characteristic color-reaction be obtained with nitric acid and ammonium, the calculus consists of uric acid or ammonium urate. A portion of the finely-powdered calculus is subjected to boiling water, when, if complete solution be effected, the calculus is ammonium urate; but if slightly or not at all solvent, it may be concluded that it is a uric-acid calculus. If further confirmation be necessary, let the solution stand until cool : ammonium will be evolved when treated with potassium hydroxid, if ammonium urate be present; and red litmus will be turned blue if suspended over the solution. If the result be negative—no ammonium present—the calculus is uric acid.

Xanthin does not give murexid reaction, but its solution in nitric acid upon evaporation leaves a bright citron-yellow residue, insoluble in potassium carbonate, but soluble in potassium hydroxid, with resulting deep reddish-yellow color.

Cystin does not give murexid reaction. Owing to its contained sulphur, if dissolved in potassium hydroxid and a little lead acetate be added, upon boiling a black precipitate of lead sulphide forms and imparts to the solution an inky appearance. Cystin also dissolves in ammonium, and upon evaporation crystallizes in regular hexagonal plates. If dissolved in hydrochloric acid and slowly evaporated, it forms diverging crystals arranged in sheaf-like form.

Protein concretions do not give murexid reaction; upon heating they evolve the odor of burnt horn or feathers. They are insoluble in water, alcohol, and ether, but are soluble in potassium hydroxid.

Urostealith gives no murexid reaction, but dissolves in ether, and yields fatty acids upon boiling with baryta-water. It dissolves in potassium hydroxid when heated and becomes saponaceous.

If the concretion be incombustible and leave, after ignition, a relatively large residue, it is necessary next to proceed to determine its composition, as follows:—

Urates of the Fixed Alkalies (*Sodium and Potassium Urates*).—In order to isolate these fixed bases the concretion is finely powdered, and after boiling in distilled water is filtered. The urates pass through the filter in solution, while the less soluble uric acid remains on the filter. The solution is next evaporated and then ignited, and the residue consists of the fixed bases. If the residue turn moistened turmuric paper brown, it is either potassium or sodium; if it be the latter, it imparts to the flame of the blow-pipe a yellow color.

Magnesium and calcium, if present in the residue, may be dissolved in dilute acids, and, upon addition of sodium phosphate and ammonium, the calcium and magnesium are precipitated as ammonio-magnesium and lime phosphates.

Calcium Oxalate.—These concretions first blacken upon heating, but upon further ignition they finally leave considerable white ash, which dissolves in hydrochloric acid *with* effervescence. If this solution be neutralized with ammonium, and oxalic acid be added, characteristic envelope-shaped crystals of calcium oxalate are precipitated, and may be recognized readily by the microscope.

Calcium carbonate, like calcium oxalate, at first blackens upon ignition, but ultimately burns white, leaving considerable infusible ash. Calcium carbonate, however, is distinguished from calcic oxalate by its highly-characteristic property of dissolving in hydrochloric acid *with* effervescence. It will be remembered that the fused ash of calcium oxalate—not the calculus—dissolves in hydrochloric acid with effervescence.

Ammonio-magnesium phosphate with more or less *calcium phosphate* usually occur together, and as such constitute the mixed phosphatic or fusible calculus. Upon ignition this calculus melts into an enamel-like mass. Upon prolonged ignition

ON HEATING THE POWDER ON PLATINUM-FOIL, IT

Does not burn	The powder when treated with HCl	Does not effervesce	The gently-heated powder with HCl	The powder when moistened with a little KHO	Abundant ammonia. The powder dissolves in acetic acid or HCl. This solution gives a crystalline precipitate with ammonia	Triple phosphate (mixed with unknown amount of earthy phosphate).
					No NH_3, or, at least, only traces of NH_3. Powder dissolves in acetic acid or HCl. This solution is precipitated by ammonia (amorphous)	Bone-earth (magnesium and calcium phosphate).
				Effervesces		Calcium oxalate.
		Effervesces				Calcium carbonate.
Does burn	With flame	Flame yellow, continuous. Odor of burnt feathers. Insoluble in alcohol and ether. Soluble in KHO with heat. Precipitated herefrom by acetic acid and generation of H_2S				Fibrin.
		Flame yellow, pale, continuous. Odor of resin or shellac on burning. Powder soluble in alcohol and ether				Urostealith.
		Flame pale blue, burns a short time. Peculiar sharp odor. The powder dissolves in ammonia, and six-sided plates separate on the spontaneous evaporation of the ammonia				Cystin.
	Without flame	Does not give murexid test. The powder dissolves in HNO_3 without effervescence. The dried yellow residue becomes orange with alkali, beautiful red on warming				Xanthin.
		The powder gives the murexid test	The powder when treated with KHO gives	Strong ammonium reaction		Ammonium urate.
				No noticeable ammonium reaction		Uric acid.

they do not show an alkaline reaction like calcium oxalate and carbonate. The fused ash of this calculus dissolves in hydrochloric acid *without* effervescence.

The excellent table on preceding page, from Heller, shows at a glance the chief features of the analysis of the various calculi, and will be found to greatly facilitate the analysis of calculus by the student.

PART II.

URINARY DIAGNOSIS.

DISEASES OF THE URINARY ORGANS AND URINARY DISORDERS.

THE URINE IN OTHER DISEASES.

SECTION IX.

DISEASES OF THE URINARY ORGANS, AND URINARY DISORDERS.

URINARY diagnosis, as considered in the subsequent pages of this work, will include: *First*, diagnostic data derivable from the urine which relate directly to pathological conditions of the urinary organs themselves. *Second*, diagnostic data derivable from the urine which relate to pathological conditions, either local or general, but the prominent feature of which is some marked and characteristic departure from the normal condition of the urine itself. *Third*, diagnostic data derivable from the urine which relate to pathological conditions primarily independent of the urinary organs, in which the latter may or may not become involved.

In order to bring the range of urinary diagnosis more fully within the field of practical clinical work, the plan will be followed of first describing the changes effected in the urine by the various forms of disease, followed by a brief epitome of the leading clinical symptoms, and, where necessary, also the differential features in each case.

A perusal of the eight preceding sections will familiarize the student with the process of secretion and excretion of the urine; the chemical and microscopical characters of the latter, both normal and abnormal; and the clinical significance of the various morbid products met with in the urine in the course of disease. In order now to compass the entire groundwork of knowledge essential for practical urinary diagnosis, it only remains to consider the most approved methods of physical examination of the urinary organs themselves. This requires a practical knowledge of the regional anatomy of the urinary organs, and, while doubtless most readers of this volume are already familiar with the subject through the numerous and excellent text-books on anatomy now in general use, it is yet believed that a brief and practical survey of the subject here will facilitate the study of the subjects shortly to be considered.

ANATOMICAL CONSIDERATIONS.

The Kidneys.—These are two large, glandular organs situated in the upper and posterior part of the abdominal cavity, on either side of the spinal column. Each kidney is about four inches in length, two inches in its transverse diameter, and rather more than one inch in thickness. These dimensions vary somewhat in individual cases. The left kidney is ordinarily slightly longer and narrower than the right kidney. The weight of each kidney is from 4 to 5 ounces, the male kidney being ordinarily 2 or 3 drachms heavier than that of the female. The left kidney in both sexes weighs about 100 grains more than the right one. The combined weight of both organs, in proportion to the body-weight, is about 1 to 240.

In form the kidney resembles a "*haricot*," or "*kidney-bean.*" It is compressed from either side, presenting an anterior and posterior surface, both of which are slightly convex, the anterior surface most so. The outer border presents an elongated convex line, while the inner border is concave, with a deep notch in the centre,—"*the hilum.*" The upper and lower extremities of the kidney are slightly wider than the middle of the organ, the upper being somewhat the wider of the two. The anterior surfaces of the kidneys look obliquely outward and forward from either side of the bodies of the vertebræ. The posterior surfaces of the kidneys—rather more flattened than the anterior—look obliquely backward and inward toward the spines of the vertebræ. The upper end of the kidney—somewhat knobbed and larger than the lower—is nearer the spinal column, and has a slightly more posterior position than the lower end. The inner border of the kidney, at its upper part, is about one inch from the middle line of the body; the outer border, at its lower part, is three and three-fourths inches from the middle line of the body. The outer or convex border of the kidney looks obliquely upward, while the concave or inner border looks obliquely downward and forward.

The kidneys are situated deep in the loins, on either side of the vertebral column. The upper border of the kidney corresponds with the space between the eleventh and twelfth ribs, while the lower border corresponds with the middle of the third lumbar vertebra. The pelvis of the kidney is about on a level with the spine of the first lumbar vertebra. During deep inspiration both kidneys are usually depressed by the diaphragm about half an inch, *though not always so.*

"An horizontal line passing through the umbilicus would lie just below the lower borders of both kidneys; while a vertical line extending perpendicularly upward from the middle of Poupart's ligament to the costal arch would pass directly over the kidney, slightly external to its median line. Posteriorly, a line parallel with and one inch from the vertebral column, extending from the lower edge of the tip of the spinous process of the eleventh dorsal vertebra to the lower edge of the spinous process of the third lumbar vertebra, would fall just inside of the inner border

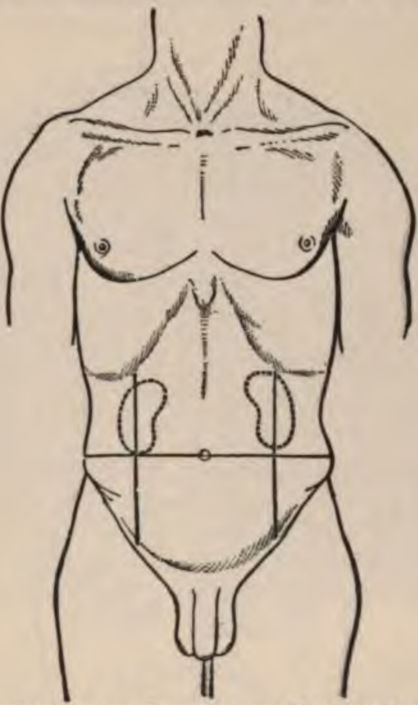

FIG. 36.—TOPOGRAPHICAL RELATIONS OF KIDNEYS, ANTERIORLY. (After Morris.)

of the kidney. If now two lines be drawn, from the ends of the line just described, horizontally outward for two and three-fourths inches, and if the outer ends of these two lines be joined by a perpendicular line, the whole kidney would normally lie within the four lines described" (Morris).

The kidneys rest on the crura of the diaphragm, on the anterior lamella of the posterior aponeurosis of the transversalis muscle. To a slight extent they also rest upon the psoas muscle. The *right kidney* is somewhat lower than the left, owing to the position of the liver, which it touches by its suprarenal capsule at its upper end; then the peritoneum passes over its anterior surface near the upper end, and the duodenum and commencement of the transverse colon are in contact with it where they are uncovered by peritoneum. The *left kidney*, rather higher

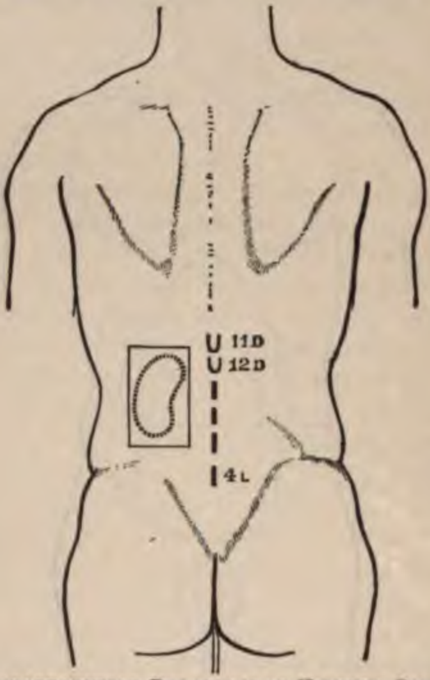

FIG. 87.—TOPOGRAPHICAL RELATIONS OF KIDNEYS, POSTERIORLY. (After Morris.)

than the right, is covered in front by the great end of the stomach, the spleen, and the descending colon. The front of the organ touches the fundus of the stomach, and then comes in contact with the pancreas and, lower down, with the commencement of the descending colon. The external border of the left kidney, in the upper two-thirds of its extent, is in contact with the spleen. (See Fig. 38.)

The kidneys are surrounded by a thick layer of fat contained in the meshes of a loose areolar tissue and constitute the "*tunica adiposa.*" It is thicker and more abundant posteriorly than anteriorly, but everywhere it completely invests the fibrous capsule of the organs. The amount of fat contained in the tunica adiposa is subject to great variation in different subjects. This

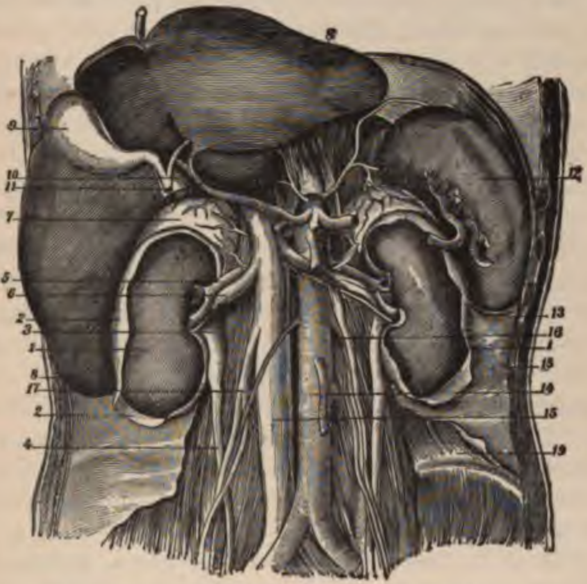

FIG. 38.—RELATIONS OF THE KIDNEYS. (After Sappey.)

1-1, the two kidneys; 2-2, fibrous capsules; 3, pelvis of the kidney; 4, ureter; 5, renal artery; 6, renal vein; 7, suprarenal body; 8-8, liver, raised to show relations of its lower surface to right kidney; 9, gall-bladder; 10, terminus of portal vein; 11, origin of common bile-duct; 12, spleen, turned outward to show relations with left kidney; 13, semicircular pouch on which the lower end of the spleen rests; 14, abdominal aorta; 15, vena cava inferior; 16, left spermatic vein and artery; 17, right spermatic vein, opening into vena cava inferior; 18, subperitoneal fibrous layer or fascia propria, dividing to form renal sheaths; 19, lower end of quadratus lumborum muscle.

fact should not be forgotten, since in stout persons it may be so pronounced as to mislead one as to the size of the kidney itself. On the other hand, in spare subjects, the fatty elements of the tunica adiposa may become so far absorbed that this tunic becomes loose, and its connections with the kidney and surrounding parts are relaxed so that the kidneys are capable of a very considerable degree of mobility.

The *capsule* of the kidney is a thin, smooth, firm, and closely-fitting envelope. Composed of numerous firm, elastic fibres, it possesses considerable power of stretching and contracting, regulated by the degree of vascular tension of the kidney. The capsule adheres, by minute fibres of connective tissue and capillary vessels, to the surface of the kidney, from which, however, it can be readily separated in the healthy organ without dragging any of the glandular structure of the organ proper with it. The capsule, following the notch or hilum in the renal substance, passes into the sinus of the kidney and becomes continuous, around the bases of the papillæ of the pyramids, with the stronger external fibres and elastic tissues of the calyces and pelvis. The *pedicle* of the kidney is composed of the dilated upper end of the ureter, the renal artery and vein, a quantity of connective tissue, and a large number of lymphatics and nerves. The relations of the vessels and ureter to each other in the pedicle are as follow: From above downward, *artery, vein, and ureter;* from before backward, *vein, artery, and ureter.* This arrangement occasionally varies.

The kidney is liberally supplied with blood; indeed, out of all proportion so, according to its relative size. The *renal artery* is of large size and arises from the aorta a little below the origin of the superior mesenteric artery, the right usually arising a little lower than the left. As the aorta lies to the left of the median line, the right renal artery is longer than the left and crosses behind the vena cava inferior. Before reaching the notch or hilum of the kidney each artery divides into four or five chief branches, which sink into the sinus behind the corresponding branches of the renal vein and in front of the pelvis. Deep in the notch of the kidney these branches break up into a number of smaller branches, which leave the veins between the calyces and enter the substance of the kidney between the papillæ.

The *renal vein* is a short, wide vessel, and, like the artery, takes an almost horizontal course. Its primary branches—four or five in number—issue from the hilum in front of the arterial branches, and then the vein continues in front of the artery until it joins the vena cava. The left renal vein is joined by the spermatic vein, both right and left renal veins receiving branches from the suprarenal capsule of their respective sides.

The *nerves* of the kidney consist of filaments from both the sympathetic and cerebro-spinal systems. They accompany the renal artery, and are derived from the renal plexus and the lesser splanchnic nerve.

The kidneys are surmounted by two small, yellowish, flattened bodies,—the *suprarenal capsules*,—which dip slightly downward over the upper borders. The right one is somewhat triangular-shaped, the left one semilunar. They are connected with the kidneys by the common investing areolar tissue, and each capsule is marked on its anterior surface by a fissure which appears to divide it into two lobes. The right suprarenal body is closely adherent to the posterior and under surface of the liver; the left lies in contact with the pancreas and spleen. Both capsules rest against the crura of the diaphragm, on a level with the tenth dorsal vertebra, and by their inner borders are in relation with the great splanchnic nerve and semilunar ganglion.

The Renal Pelvis.—As the ureter passes upward it loses its cylindrical form on a level with the lower end of the kidney, and it there begins to expand into a large, funnel-shaped dilatation, which is known as the "*pelvis*" of the kidney. After entering the hilum or notch the pelvis divides into two or three primary tubular branches, which in turn end in several short truncated but wide pouches, named *calyces* or *infundibula*, the mouths of which receive the papillæ as "does a glove the fingers." A single calyx often surrounds two or three papillæ, so that the calyces are fewer in number than the pyramids of the kidney.

The Ureter begins at the lower, pointed end of the funnel-shaped renal pelvis, at a point about the level of the lower border of the kidney, and extends, in length from fourteen to sixteen inches, to the base of the bladder, into which it opens by a constricted, slit-like opening, after having passed obliquely for nearly an inch between its muscular and mucous coats.

The ureter is a cylindrical, membranous tube, about the diameter of a goose-quill; but the lumen of the tube is not uniform. The ureter, in passing downward and inward to the brim of the pelvis, lies directly behind the peritoneum, resting on the psoas muscle, and is crossed by the spermatic vessels. In the pelvis it enters the peritoneal fold constituting the posterior false ligament of the bladder, and runs downward and forward by the side of the bladder, entering the wall of the latter about two inches from the ureter of the opposite side. In the female the ureters pass by the neck of the uterus, about an inch from the latter.

The Bladder.—This is a hollow, musculo-membranous organ situated behind the pubis within the pelvis, in front of the rectum in the male, the uterus and vagina intervening between it and the rectum in the female. The shape of the bladder varies with the age, sex, and degree of distension of the organ. In infancy it is conical in form and projects above the pubis. In the adult, when empty, it is small and triangular in form, situated deeply in the pelvis, flattened from before backward, and rises on a level with the upper border of the pubic symphysis. When *slightly* distended, the bladder is rounded in form and partly fills the pelvis; when *greatly* distended it is oval in shape and rises into the abdominal cavity, sometimes extending as far as the umbilicus. It is largest in its vertical diameter, and its long axis is directed obliquely downward and backward. When moderately distended (containing one pint) it measures about five inches in length by about three inches in width. The bladder is divided into summit, body, base, and neck. The summit constitutes the upper, rounded border of the organ, which is covered by peritoneum. The body of the bladder, posteriorly, is also covered by peritoneum, but anteriorly it is uncovered by that membrane. The base of the bladder is directed downward and backward, resting, in the male, upon the rectum; in the female, lying in contact with the lower part of the cervix uteri, and adherent to the anterior vaginal wall. The neck of the bladder is the constricted portion continuous with the urethra; in the male, surrounded by the prostate gland.

Physical Examination.

For examination of the *kidney* by means of percussion the patient should lie upon the abdomen, across a rather hard pillow. In this position there will be found, in the lumbar region of the normal subject with normal kidneys, a space between the last rib and the pelvic brim, rather less than two inches broad,—five centimetres,—which elicits a dull note upon sharp percussion. Anteriorly, this dullness is abruptly exchanged for tympanitic resonance as the intestines are approached. The dull note is continuous upward and outward beyond the limits of the kidney: on the right side continuous with that due to the liver; on the left side continuous with that due to the spleen; while below, the pelvic brim (within which the lower border of the kidney lies) prevents the lower border of the kidney from being defined. It will, therefore, be seen that the *normal kidney* elicits but little information upon percussion, owing to its unfavorable position for that purpose, for even moderately-enlarged kidneys cannot, with percussion, be thus outlined. "Obscured by the thickness of the abdominal walls, covered in part by the lower ribs, liver, and spleen, in part arched over by the vertebral processes, covered by the body of the sacro-spinatus muscle, the lateral border of which closely corresponds with the convex border of the kidney, it will be readily seen that these organs present the greatest obstacles to percussion." In abnormal conditions of the kidney, however, notably those of large tumor, percussion becomes of very decided utility, but for such purposes the patient should be placed upon the back, in the position for palpation.

Palpation of the kidney is best conducted by placing the patient upon the back, with the thighs slightly flexed and somewhat separated from each other. The examiner should approach the side of the patient which he desires to palpate, and with one hand upon the anterior wall of the abdomen he should pass the other hand behind the patient, pressing deeply with his fingers from behind forward in the renal region (between the lower border of the ribs and the iliac crest), pushing firmly forward any tumor against the opposite hand.

In pathological conditions of the kidneys, notably if the organs be very much enlarged or displaced, physical examination often elicits valuable diagnostic information. Thus, in the case of morbid growths, some knowledge of their nature is obtainable by the sense of touch and manipulation. Thus, the organs may feel smooth, uneven, globular, lobulated, fluctuant, soft, or dense. They move but slightly with respiration. If tumor be present, the kidney may leave its normal bed beneath the diaphragm and be seen in front; but a *normal* movable kidney is not visible upon anterior inspection.

A circular, symmetrical swelling between the borders of the ribs and the pelvic brim, extending posteriorly toward the spine, with œdematous condition of the skin and tissues beneath, may point to perinephritis with perinephritic abscess. Tenderness upon pressure is obtainable in acute, but rarely, if ever, in chronic, diffuse nephritis. It is present in renal stone, especially if the latter has excited inflammation. In hydronephrosis it is usually present, and in perinephritis it is especially prominent. Large formations, as carcinoma, sarcoma, hydronephrosis, pyonephrosis, perinephritis, and echinococcus, are plainly palpable; the latter may show, by quick, short, bimanual percussion-strokes, a peculiar whiz,—the "*hydatid vibration.*" Since the kidney lies behind the peritoneum, when it becomes enlarged by growths so as to extend forward it usually pushes before it the ascending or descending colon against the anterior abdominal wall; in such case the colon may be made to furnish valuable differential knowledge, because other abdominal growths, being intra-peritoneal, push the colon aside, and therefore furnish no tympanitic note from this source. Since the colon is best distinguished when it contains air, it is often advisable to inflate it for diagnostic purposes. Movable kidney is known by its form, mobility, size, often its capability of replacement, and occasionally pulsation of the renal artery may be felt.

Although palpation is usually sufficient to reveal the presence of renal tumors of any considerable size, *anterior* or *lateral* percussion is usefully employed for confirmative purposes. In the author's experience, one of the most valuable methods is that of anterior auscultatory percussion for this special purpose. By placing the stethoscope over the centre of a viscus or tumor, and by the finger-tips *very gently* tapping the abdominal wall in a radiating direction from the instrument, the outline of the body upon which the stethoscope rests can be made out with great precision by the impulse and pitch of the note conveyed to the ear.

The method of diagnosticating unilateral dislocation of the kidney by bilateral percussion, upon the theory of differential bilateral resonance, although formerly much relied upon, has, upon wider experience, proved untrustworthy.

The differential features between renal tumors and those of adjacent organs often require most careful consideration. Thus, the differential features between a moderately displaced right kidney downward and a distended gall-bladder, an echinococcus cyst or other growth upon the lower border of the liver is not readily made out by palpation or percussion. Respiratory mobility, if pronounced, may, with considerable degree of certainty, exclude the kidney. Capability of replacement, on the other hand, so that the tumor disappears, proves the tumor to be renal. Movable left kidney is differentiated from movable spleen by palpation and percussion. Palpation may reveal characteristic notches in case of the spleen; while in movable kidney the pulsations of the renal artery may sometimes be felt by deep pressure at the hilum of the organ. The course and relations of the colon, as ascertained by percussion, are also here valuable guides. Respiratory mobility may or may not accompany splenic enlargement; if present it argues against the renal nature of the tumor.

The ureters are so inaccessible that they furnish but little information upon palpation or percussion. A few surgeons, notably Simon, have repeatedly felt the ureters by anæsthetizing the patient and introducing the hand into the rectum. Recently palpation of the ureters *per vaginam* has come to be practiced. This offers no special difficulty, as the ureters can be plainly felt for nearly three inches of their lower extremities, and growths or stones in this portion of the canal can be clearly made out. To a less extent palpation of the ureter may be practiced *per rectum* with the finger, but only about the last inch or so of the tube can thus be ordinarily defined, as it lies within the bladder-wall.

Abdominal palpation is rarely successful in ureteral examinations, and only in cases of very spare subjects, when the ureters are greatly distended or are occupied by large growths. The vesical orifice of the ureter may be inspected by means of the cystoscope, and morbid conditions of that part of the canal can be determined satisfactorily. Catheterization of the ureters, as yet, is applicable only to limited cases—in the female. This immensely valuable means of diagnosis, especially desirable for renal as well as ureteral purposes, must very shortly be perfected in connection with the cystoscope. The author's instrument, devised by Leiter for this purpose, has never proved satisfactory; nor can any of the instruments in present use be depended upon to meet the purpose.

The bladder is only noticeable on external inspection in cases of extreme distension, when it rises into the abdominal cavity. Palpation is applicable in moderate distension of the bladder above the symphysis pubis. It may also be practiced *per vaginam* and *per rectum* either by one hand or, often with advantage, bimanually. Sir Henry Thompson proposed and practiced digital exploration of the bladder by opening the urethra at or about the membranous portion and making a passage sufficient to admit the index finger into the bladder. While the operation is in itself usually a harmless one, more recent measures (the cystoscope) for the most part render it unnecessary. Percussion over the region of the bladder reveals an area of more or less extended dullness, according to the degree of distension of the organ. But percussion of the bladder for the purpose of distinguishing tumors of the vesical region is scarcely necessary, since catheterization will usually quickly determine if they be of vesical origin or not.

A very decided advance in our methods of inspecting the bladder has taken place since 1887, when Nitze first published his methods of examination of the bladder by means of electric illumination.[1] Since then the complete work of Fenwick on "Electric Illumination of the Bladder and Urethra" (1888) and Nitze's "Text-Book of Cystoscopy" (1889) have furnished in detail all the technique of this method of examination of the bladder. By means of the cystoscope we are now able to obtain most complete knowledge of a large number of pathological conditions of the bladder. "Its use plainly discloses ulcerations, their character and extent. It enables us to see diverticula, to find and locate foreign bodies, to not only plainly see stones, but also to ascertain their size, number, shape, character, and even to percuss them with the instrument, the encysted stones no longer escaping detection. Above all, the diagnosis of morbid growths of the bladder by this means is rendered comparatively easy and sufficiently early to render far more efficient their treatment." Certainly, no longer can a diagnosis of obscure disease of the bladder be considered complete without the use of the cystoscope.

RENAL HYPERÆMIA.

Hyperæmia of the kidneys is met with in two forms: (*a*) *active or acute hyperæmia*, consisting of active determination of arterial blood to the kidneys; (*b*) *passive hyperæmia*, or venous stasis, consisting of a retention of venous blood in the kidneys, usually the result of some obstruction to the venous circulation, either local or general.

ACUTE RENAL HYPERÆMIA.

This condition may be said to mark the initial stage of nearly all forms of acute nephritis. It may be brought about by numerous causes. In the course of eruptive fevers and inflammatory diseases, such as diphtheria, erysipelas, pneumonia, and acute rheumatism, the kidneys, in common with other internal organs, become more or less pronouncedly hyperæmic. Toxic influences and certain irritants are very common causes of renal hyperæmia. If the toxin or irritant be quickly removed, the normal condition of the renal circulation is rapidly established again; but if protracted sufficiently long, the prolonged hyperæmia is very apt to result in active nephritis.

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[1] "Contribution to Endoscopy of the Male Bladder," Archiv f. klin. Chir., vol. xxxvi, p. 661.

A number of substances when swallowed are capable of inducing active renal hyperæmia, the best known of which are cantharidis, turpentine, sulphuric and other mineral acids, phosphorus, cubebs, and potassium chlorate. Acute renal hyperæmia may also be induced by local auto-irritation, as in the case of lithuria and oxaluria when long continued. Exposure to cold and moisture constitutes a frequent cause of the condition under consideration. In the majority of such cases the hyperæmia subsides without, perhaps, having attracted special attention, but sometimes it passes on into acute nephritis. In late stages of diabetes the kidneys usually become hyperæmic, and even albuminuria and mild grades of nephritis may also result.

The Urine.—In acute hyperæmia of the kidneys the urine contains more or less blood, the quantity depending upon the degree of congestion present. In mild cases only a few scattering corpuscles are to be seen, while in active congestion the urine may be very bloody. The color of the urine will depend mostly upon the degree of hæmorrhage. Albumin is always present, but usually in small amount, rarely exceeding 10 or 15 per cent. bulk measure. The urine usually contains a few renal casts, mostly of the hyaline order, and of small size; and free epithelium from the renal tubules may often, though not invariably, be observed. The quantity of urine at first is increased, and, corresponding to this, the specific gravity is somewhat reduced, and the proportion of solids is reduced, though the absolute solids may be normal. The urine retains its normal acidity.

If the congestion continue long, most of the physical characters of the urine just named are apt to become reversed. The specific gravity becomes increased, as do the solids, while the quantity becomes diminished. In some cases of acute renal hyperæmia, especially when induced by cantharidis, fibrinous coagula may appear in the urine.

Leading Clinical Features.—When the cause is toxic, the symptoms are to be looked for in the resultant effects on other organs of the substance ingested. Locally, more or less frequency of micturition is present, sometimes with pain, urgency, and perhaps vesical tenesmus. Some pain is apt to be present in the region of the kidneys, but, in the absence of this, some tenderness may usually be elicited upon deep pressure in the same location. In febrile forms the usual features of pyrexia are to be observed, more or less marked, according to the grade and character of the fever present.

PASSIVE RENAL HYPERÆMIA.

Venous stasis or passive hyperæmia of the kidneys is not at any time a primary renal disease, but is always secondary to some obstructive disease of the heart or circulatory organs. Mitral disease of the heart and valvular insufficiency, or stenosis, are the active causes of most of these cases.

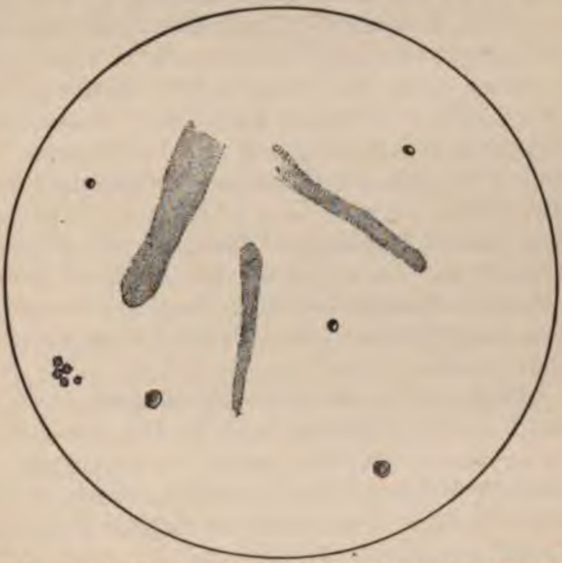

FIG. 39.—URINARY SEDIMENT IN PASSIVE HYPERÆMIA OF THE KIDNEYS. (After Peyer.)

The Urine.—The quantity of the urine in uncomplicated cases is always diminished, and the specific gravity is increased, usually ranging from 1025 to 1030. The color of the urine is dark brownish-red, and the chemical reaction is frankly acid. The transparency of the urine is somewhat diminished, owing to the presence of undissolved urates and increase of mucus. The quantity of uric acid is relatively, and sometimes absolutely, increased, and free uric-acid crystals are usually to be seen in the sediment, as are the amorphous urates. There is usually no reduction, either in the relative or absolute quantity of urea present. The urine usually contains a small and variable amount of albumin; sometimes merely traces are present; occasionally, though rarely, it is absent, while sometimes it may reach one or two grammes per litre; the degree of stasis, seemingly, does not correspond with the degree of albuminuria. The sediment usually contains a few hyaline casts of small size, and, occasionally, scattering blood-discs or nuclei may be seen attached to these casts (Fig. 39). A few scattering blood-corpuscles are usually to be seen in the sediment; occasionally this is considerable, although such is more rarely the case than the appearance of the urine would indicate, owing to the concentration of the urine.

Leading Clinical Symptoms.—These are very characteristic, and comprise dropsy, mostly of the feet and lower extremities; general cyanosis, dyspnœa, hacking cough; prominence of the large veins, notably those of the abdomen; weak, thready pulse, and cardiac lesions.

Differentiation.—Venous stasis of the kidney is to be distinguished from interstitial nephritis by the increased volume of the urine in the latter disease, its low specific gravity, pale color, normal transparency, spare deposit; absence, as a rule, of blood from the deposit, and constant deficiency of urea, both relatively and absolutely. To these may be added, as the most prominent clinical features of interstitial nephritis, a full, hard pulse, *always* showing increased tension; cardiac enlargement (left ventricle hypertrophied), visual disorders in late stages, absence of dropsy till very late, chronic uræmic disturbances, and the habit of nocturnal micturition,—all of which are absent in passive renal hyperæmia.

ACUTE DIFFUSE NEPHRITIS.

This is the so-called acute Bright's disease, and is marked by very pronounced and characteristic features, clinically as well as urinary. The causes include those already considered as provocative of acute renal hyperæmia, any of which, if of sufficient intensity or duration, are capable of bringing on acute diffuse nephritis. Of the use of toxic drugs, as a matter of actual experience, acute nephritis is rarely thus induced, probably because the exciting cause is rarely prolonged sufficiently to bring about high grades of nephritis. Acute diffuse nephritis is most often met with in practice as a result of the acute infectious fevers, notably scarlatina, pneumonia, typhoid fever, diphtheria, relapsing fever, and epidemic influenza. Less often violent exposure to cold and certain local affections of the skin, including extensive burns, erysipelas, carbuncles, etc., give rise to this disease. Lastly, pregnancy must be recognized as the causative factor of a very considerable number of these cases.

The Urine.—In acute diffuse nephritis the urine possesses the following typical characteristics: The quantity is invariably diminished, and sometimes extremely so. At the height of the disease but a few ounces of urine may be voided during the whole twenty-four hours; but later on, if improvement occur, the quantity gradually increases until the normal volume, or even more, may be reached. If the quantity of urine rise above the normal it may be taken as an evidence that the acute character of the disease is modified, and the tendency is toward resolution. On the other hand the urine, at the very height of acute nephritis, may become practically suppressed, and, if this continue, death may be invariably predicted within a very few days.

The specific gravity of the urine depends upon the quantity voided, and, as already shown, this varies with the course of the disease; so will this feature of the urine. In the early and very acute stage of the disease the specific gravity of the urine usually rises above normal, often reaching 1025 to 1030 or even higher. With continuance of the disease the tendency is toward a lowered specific gravity of the urine, corresponding with the increased volume.

The color of the urine varies considerably at different periods of the disease, the variation depending in part upon the quantity of urine voided, and in part upon the quantity of contained blood. As a rule, the color of the urine is dark, more or less approaching chocolate color. The transparency of the urine is diminished, the urine presenting a smoky, opaque appearance, in which the normal lustre is completely lost. A diminution of this character of the urine denotes changes tending toward resolution. The chemical reaction of the urine, uninfluenced by medication, is always sharply acid; but upon the use of alkaline salts, so much employed in treatment, the urine is often found to be alkaline.

The gross quantity of the urinary solids is diminished in acute nephritis, the urea suffering the most pronounced reduction. The relative amount of solids varies with the volume of urine excreted; so that in the early stage, marked by great reduction in the volume of urine, the relative amount of solids may be normal or above. It is important to make the distinction here, however, that the gross solids for twenty-four hours are always reduced. Upon convalescence the gross solids are increased, especially the urea and chlorides, which were merely held back. At the height of the disease the urea is often reduced to 100 grains or even less for twenty-four hours. The urine contains albumin in variable, but always large amount in acute nephritis. It may reach as high as 2 per cent., or even more by actual weight; so that upon coagulation it nearly fills the test-tube. More frequently, however, the range is in the vicinity of ½ to 1 per cent.;—5 to 10 grammes per litre (Esbach's method). A few cases of acute nephritis following scarlatina are recorded, in which the urine was free from albumin. It is, however, rare in such cases that albuminuria is absent throughout the whole course of the disease; more often it is of sudden onset at some stage, and occasionally it has been observed in intermittent form.

The degree of albuminuria is considered to mark the degree and course of acute nephritis toward a favorable or unfavorable termination; and while the degree of albuminuria can rarely be taken as a safe guide in this direction in general, it may be more depended upon as such in this special form of nephritis than perhaps in any other form of renal disease. On the whole, a continuous diminution in the quantity of albumin in the urine in acute nephritis may be accepted as evidence of progress toward resolution.

The presence of blood in the urine may be regarded as one of the essential features of this disease, though varying greatly in amount in different cases as well as at different periods in the same case. Fluctuations are frequent during the course of the disease, and, indeed, the blood may alternately appear and disappear. Hæmaturia is developed early, being in most cases among the first symptoms noticed, while it usually subsides much earlier than does albuminuria. The quantity of blood lost in the average case of acute nephritis is very considerable if the disease continue long; this is partly evident by the increasing pallor of these subjects. Hæmaturia may be regarded as a valuable prognostic indication in this disease, being rarely absent in severe cases; its appearance marks, with early and great certainty, relapses of the acute process, when previous progress was favorable.

The urinary sediment in acute diffuse nephritis is large in quantity, usually brownish in color from admixture with blood, urates, and coloring matters. Microscopical investigation of the sediment discloses the presence of red blood-corpuscles in larger or smaller numbers. These are somewhat altered, and appear "*washed out*" and ragged, unless in cases of marked hæmorrhage, when they present more nearly their normal appearance. Some pus-corpuscles are to be noted in the field, but rarely in any considerable number. Cellular forms are characteristic of this deposit; mostly small, round, uninuclear cells from the renal tubules, which may be present in great numbers; while less numerous are the narrow-pointed, small-tailed cells from the renal pelvis. The epithelium is well preserved, and affords characteristic pictures of these structures under the microscope. Renal casts are present in large numbers, and may have attached to them (*a*) blood-corpuscles, (*b*) leucocytes, (*c*) renal epithelium (Fig. 40). The above varieties of casts are characteristic of the beginning of acute nephritis, or the disease at its height; but they are subject to alterations in character as the disease continues some time. With advancing changes consequent to the disease, disorganization of the epithelium occurs, and we find the metamorphosed casts, such as the dark, granular, and broad, hyaline ones, with more or less organic molecular *débris*. With advance toward resolution the quantity of sediment diminishes and the casts become less and less numerous. As already noted, the uric acid of the urine is increased in acute nephritis, the chlorides are diminished, and in very acute cases the latter may disappear altogether. When advancing toward recovery the volume of urine increases, and with this diuresis the chlorides and urea become markedly increased, having been held back by defective eliminative power of the kidney during the height of the disease.

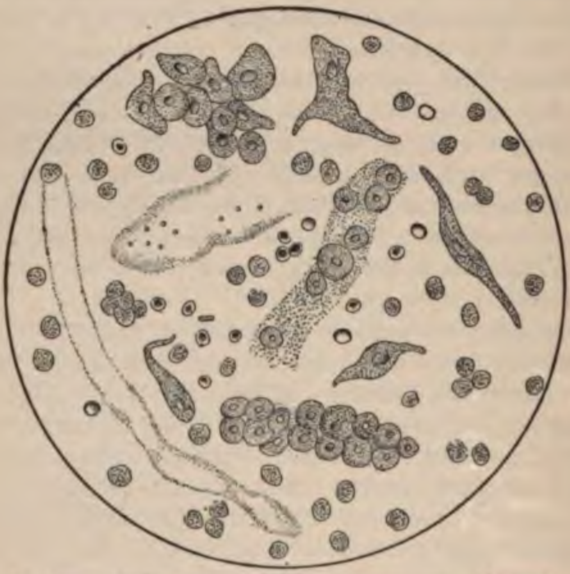

FIG. 40.—URINARY SEDIMENT IN ACUTE NEPHRITIS. (After Peyer.)

Leading Clinical Features.—The most prominent clinical features of typical acute diffuse nephritis are as follow: Dropsy, which is always present, and of a general character, involving the face, hands, feet, and cellular tissues in general. A very noticeable pallor steals over the patient, though less prominent than in the chronic form of the disease. The temperature rises to 100° or 102° F., and the pulse is over 100, full, resisting, and marked by increased tension. Headache is present, often severe, persistent, and most often frontal. Nausea is frequent and often attended by vomiting. Acute uræmia is common, often manifested by acute visual disorders, stupor, temporary paralysis, and sometimes convulsions. The appetite is abolished, thirst is prominent, and there is dull, aching pain or stiffness felt in the loins and tenderness upon deep pressure in the renal region.

CHRONIC DIFFUSE NEPHRITIS.

This disease may be a sequel of the acute nephritis just considered, but more often it develops insidiously from the beginning. It is more apt to result from the acute form when the latter is the outgrowth of scarlatina, pneumonia, diphtheria, or some of the acute infectious fevers. The student is advised to make a most careful differential study of this disease, more especially with regard to amyloid disease of the kidney, with which it has since the days of Bright himself been frequently confounded, with disastrous results to the treatment, since they are almost diametrically opposite in character.

The Urine.—The quantity of urine, as a rule, is diminished in progressive chronic diffuse nephritis. Although no such marked reduction occurs as in acute nephritis, yet a reduction of 40 or 50 per cent. of the normal volume is not uncommon. The fluctuations of the daily quantity are marked, more so than in the acute disease. In the late stages the volume of urine increases, and in chronic cases tending toward secondary contraction of the kidney the quantity of urine often exceeds the normal amount. This is because interstitial changes have been set up and the symptoms tend to conform to the interstitial variety of nephritis. The specific gravity of the urine is below normal. In cases marked by unusual reduction in the quantity of urine, the specific gravity may rise above normal. This, however, is unusual, and results from concentration of the urine. With a normal volume of urine, and often much less, the specific gravity rules below 1020, and in late stages tending toward renal contraction the specific gravity of the urine often sinks to 1010 or below.

The color of the urine varies from pale lemon to dark brown, more often approaching the former than the latter color. The urine is always cloudy, the more so as the quantity is diminished. When the volume of urine is nearly normal the color is often very light, but the transparency is always diminished more or less, the appearance of the urine being of a hazy, dirty character. This depends upon the invariable presence in the urine of a large amount of sediment, consisting of epithelium, renal casts, pus-corpuscles, and molecular matter.

The urine always contains albumin, and usually in large quantities. In fact, albuminuria may be said to reach its maximum as a symptom in this form of disease, often reaching as high as 3 or even 4 per cent. by actual weight. In such cases coagulation becomes so pronounced with reagents that an accurate estimate of the quantity by bulk measurement can only be made by largely diluting the urine previous to testing. While the average quantity of albumin in the urine in this disease, therefore, ranges very high, it fluctuates markedly in different cases as well as in the same case from time to time. It would seem to maintain a fairly constant ratio to the specific gravity of the urine in most individual cases; more especially so when the changes in the specific gravity are sudden, or are observed over short periods of time. Thus, if the specific gravity of the urine be 1014 one day, while the next day it rises to 1018, a decided increase in the amount of the albumin is sure to be noted. These changes, however, are only relative; the absolute loss of albumin for twenty-four hours remains pretty uniform over short periods of—say—a few days. Any decided increase in the absolute quantity of albumin in these cases indicates an extension or aggravation of the disease. In cases characterized by great chronicity, more especially in those cases tending toward contraction of the kidneys, the quantity of albumin in the urine often becomes reduced both relatively and absolutely.

The solids of the urine suffer more or less reduction in this disease, urea and the chlorides most notably so. Occasionally, when dropsy is subsiding under diaphoretic measures, there may be a temporary increase of the solids of the urine, especially that of urea, which may even exceed the normal. This, however, is of brief duration, and, after a time, falls back again below the normal standard.

The urinary sediment furnishes the key to the diagnosis of this disease. As already stated, the sediment is relatively large in quantity and consists of casts, white blood-corpuscles, epithelium, and cellular remnants. The casts are numerous and of nearly all known varieties, but the most distinctive ones are the *dark granular*, *broad hyaline*, and more especially the so-called *fatty casts* (Fig. 41). In the more recent cases the casts may be less numerous, and, as a rule, the hyaline, slightly dotted, or faintly granular ones, as well as those dotted with cell-fragments, predominate. The longer the disease continues, the more numerous the casts become, and, moreover, the more predominant become the dark granular casts, the broad casts from the large, straight tubes, and the casts with fat-droplets attached to them.

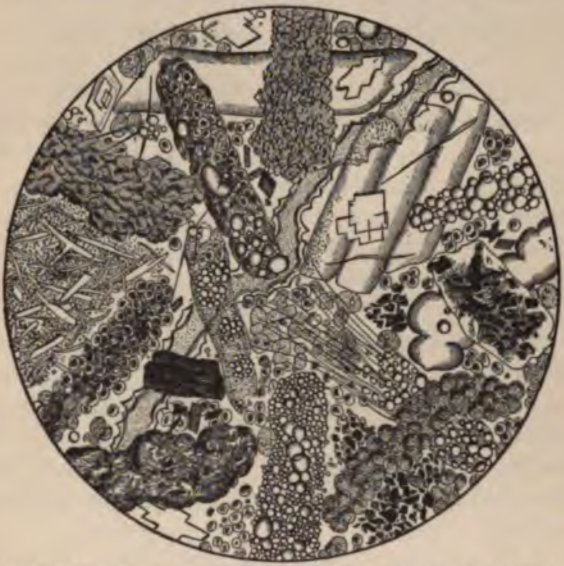

FIG. 41.—URINARY SEDIMENT IN CHRONIC DIFFUSE NEPHRITIS, SHOWING RESULTS OF FATTY CHANGES IN PROGRESS. (After Peyer.)

The fatty casts may almost be said to be characteristic of this condition. Red blood-corpuscles are rarely met with in this lesion, perhaps only in cases which have recently sprung from the acute form of nephritis. On the other hand, leucocytes are always to be found in larger or smaller numbers. A very marked sediment of granular *débris* is observed in this lesion, consisting of broken-down cellular elements.

Epithelial cells from the renal tubules are to be found, sometimes in numbers. They are less perfectly preserved than in the acute lesion, disorganization of structure being everywhere apparent.

Leading Clinical Features.—The leading clinical features of chronic diffuse nephritis are briefly and concisely the following: First and most prominently dropsy, which is progressive, obstinate, general, and sooner or later extreme,—involving the cellular tissues and ultimately the serous cavities. Anæmia is no less marked and striking, palpable in the pallid, puffy face and dough-like extremities and body, and pale mucous surfaces wherever visible. Debility is prominent and progressive; these patients being feeble and helpless, often bedridden. Emaciation is progressive, but masked by the dropsy. The appetite and digestion fail, owing to the charged condition of the blood with effete products which the kidneys fail to eliminate. Uræmia, when present, is of the less active or chronic order, coma and convulsions being rare, except at the close or the result of acute complications.

Chronic Interstitial Nephritis.

Under the above head will now be considered the diagnostic features of those usually slowly-advancing chronic processes, which ultimately terminate in granular contraction or atrophy of the kidneys, known as renal cirrhosis or chronic Bright's disease. Many of the early writers seem to have confounded this lesion with diffuse nephritis, at least so far as to consider it the outgrowth of that primary lesion. We now know that while renal contraction is sometimes the result of long-continued diffuse nephritis, yet the overwhelming majority of cases begin not only independently of that lesion, but are essentially interstitial and atrophic processes from the beginning, and, moreover, are the outgrowth of totally-opposite conditions of the system and habits of life from those in chronic diffuse nephritis. The previously robust, hearty, and overnourished are almost invariably the subjects of the interstitial lesion; while, for the most part, the opposite class of people are more commonly the subjects of the other-named lesion.

It may be premised that primary interstitial nephritis is one of the most stealthy and insidious of all diseases in its manner of approach, giving rise to few, if any, noticeable symptoms until in progress for a number of years,—often ten to fifteen. The lesions, though wide-spread, including the heart and arterial system, are yet almost imperceptible in their manifestations in the early stages; at the same time they are slowly progressive and permanent in character. Notwithstanding all this, with due care and minute scrutiny of all the surrounding features of the case, interstitial nephritis may always be diagnosticated, however early and slight the lesion, if only attention be called to the matter; and the method of compassing this will now be considered.

In the study of interstitial contracting kidney it should be borne in mind that, as a rule, it is accompanied by a progressive hypertrophy of the left ventricle of the heart in at least 80 per cent. of the cases. While the cardiac hypertrophy is in progress, the symptoms, both urinary and general, are pretty uniform and invariable. If the patient survive sufficiently long, however, the hypertrophied heart undergoes degenerative changes, and with the consequent heart-failure many of the characters of the urine, as well as the general symptoms, change completely. If this fact be kept in mind it will serve to prevent the confusion so apt to arise in consequence of the variability of the symptoms in different cases, as well as in the same case at different periods of the disease.

The Urine.—In typical interstitial nephritis the urine is increased in quantity, is slightly paler than normal in color, perfectly transparent, rather sharply acid in reaction, and the specific gravity somewhat below the normal range. Albumin is usually present in small quantity; only a few scattering casts are present, and these are of the narrow, perfectly hyaline order; renal epithelium and cellular elements are rarely observable, but uric-acid and calcium-oxalate crystals are often to be seen under the microscope. The chlorides of the urine are nearly normal in quantity, the urea more or less deficient, and the phosphates are reduced considerably.

A more minute analysis of these features shows the following characters: The quantity of urine is usually increased from the beginning. This polyuria is maintained uniformly and progressively until a comparatively late period of the disease, when heart-failure sets in and the volume of urine often then sinks below normal; nor can it in such cases again be maintained regularly up to the normal standard during the remainder of the patient's life. The specific gravity of the urine becomes progressively lowered; in the beginning a falling off of but two or three points is usual; later on the reduction is more marked, though it never descends as low as in chronic diffuse nephritis or amyloid disease, but in pronounced cases it ranges between 1010 and 1016. With heart-failure and consequent diminution of the volume of urine the specific gravity rises somewhat, and may even approach again the normal standard, after having remained for years constantly reduced.

While albuminuria is the rule in this lesion, many exceptions have been noted. The exceptions are often apparent rather than real, because albuminuria of interstitial nephritis is notoriously intermittent in character, sometimes disappearing for days and weeks, to return again and again, regardless of the stage of the disease. It is probable that if these so-called non-albuminuric cases were kept under constant observation albumin would be found in the urine in many of them some time during the course of the disease. This has been the experience of the author, although he has met with a few cases in which the urine was absolutely free from albumin throughout. So long as interstitial nephritis remains uncomplicated the quantity of albumin in the urine is invariably small, usually ranging below 10 per cent. volumetric measurement by the author's centrifugal method. General or local disturbances, such as "*catching cold*," mild febrile attacks, etc., quickly increase the albuminuria. In late stages of this lesion associated with cardiac failure albuminuria becomes augmented considerably, the quantity of albumin may reach from 30 to 40 per cent. bulk measure. In no case, however, does albuminuria approach the extreme grade in this lesion that it does either in acute or chronic diffuse nephritis.

Both the relative and absolute amount of urea in the urine begins to suffer reduction from the beginning. At first it is slight, but as the disease advances it becomes a constant and, in many cases, a marked feature. It is not at all uncommon, in advanced interstitial nephritis, to note a reduction of the absolute amount of urea of from 50 to 75 per cent. More or less reduction is also to be noted of the quantity of all the urinary solids, the chlorides suffering the least reduction and the phosphates most. With regard to the phosphates in particular, a diminution in quantity of the phosphates in the urine may be regarded almost as constant a feature of this lesion as the presence of albumin.

Casts from the renal tubules are probably always present in the urine in this lesion, but they are rarely numerous, sometimes extremely sparse and difficult to find. This is due to the fact that they are of such delicate, hyaline, non-refracting character that the most careful search is necessary to detect them; besides, their small numbers, rendered still more sparse by the accompanying polyuria, it often becomes necessary to concentrate the sediment in order to find them. As the disease advances the casts become more numerous, and often they show fine granulations; they are largely of the narrow hyaline and granular orders.

The crystalline deposit in the urine in this lesion consists chiefly of uric acid and calcium oxalate, both of which are often to be noted together. For the most part these deposits are noticeable in the early stages of the disease. The uric acid is precipitated chiefly in consequence of the diminished pigmentation of the urine in this lesion, rather than in consequence of the excess of the former. The oxalic deposit occurs most often in gouty subjects.

On the whole, the urinary sediment in this lesion is remarkably small in quantity and practically free from cellular elements, save those that are common to normal urine. It is not unusual to find, even upon standing twenty-four hours, or centrifugation of the urine, little or no sediment noticeable to the naked eye. Toward the termination of the disease, however, a sediment is usually noticeable, in consequence partly of the more concentrated state of the urine, as well as the wider extension of the lesion.

Interstitial nephritis renders the kidneys extremely prone to take on subacute or even acute attacks of nephritis upon exposure to certain causes, especially that of cold and febrile or inflammatory diseases. In such cases the quantity of albumin in the urine becomes markedly increased, the volume of urine diminished, and the sediment becomes more pronounced and approaches, in its special features, those of acute nephritis already described. In such cases it is necessary, in addition to the urinary examination, to carefully regard the history and general clinical features of the case, in order to diagnosticate the true conditions present.

Leading Clinical Features.—In typical cases of chronic interstitial nephritis we may look for the following clinical features: The patient habitually rises at night once, twice, or oftener to void urine which, to the eye, appears normal in its transparency and nearly so in color. The pulse is *always* full, hard, and resisting to the finger, and marked by decided tension as measured by the sphygmograph. The second cardiac sound, as heard best in the second right intercostal space, within an inch and a half of the sternum, is *always* distinctly accented,—sharper and louder than normal. In most cases—at least 80 per cent.—the normal area of cardiac dullness is more or less extended below and to the left, and, in many cases, notably if the lesion be advanced, this feature is very prominent. Disorders of vision are common some time during the course of this lesion, not very frequently early, but almost certain in late stages. Uræmic disorders are encountered during the course of the disease in some of the following forms: Mild post-cervical neuralgia is very common, almost characteristic; diarrhœal attacks, which mark eliminative efforts of the system vicariously; dyspnœa, which often appears of an asthmatic type; drowsiness, coma, and sometimes convulsions.

Attacks of bronchitis are common and difficult to get rid of; winter cough of the aged frequently owes its origin to this cause. Acute inflammations of the pleura, lungs, or peritoneum are prone to be suddenly kindled and run a fatal course. Dropsy is absent, save in advanced cases, and then it is due rather to the cardiac failure than to the renal lesion.

The early diagnosis rests upon the following points: A previous condition of robust health is usual; age, over 40 years; patient rises habitually at night to void urine of normal appearance; the pulse is full and hard (never weak); the second sound of the heart is abnormally loud; the urine is deficient in urea; small quantities of albumin are usually present, and hyaline casts are to be observed under the microscope if the sediment be concentrated.

The diagnosis of the advanced lesion can scarcely be overlooked by the most superficial observer. The plainly-observable hypertrophy of the heart; the presence of uræmic disorders, as headache, dyspnœa, visual defects, diarrhœal attacks, and perhaps drowsiness at times; together with certain changes in the urine, notably albuminuria, deficiency of urea, the presence of casts of the hyaline and granular order almost exclusively, serve both to call attention to the disease and mark its special character.

Interstitial contracting kidney in many of its features is not unlike passive hyperæmia of the organs. The differential features of the two have already been noted in connection with the description of the latter. (See page 245.)

AMYLOID DISEASE OF THE KIDNEY.

Amyloid change in the kidney is a local manifestation of a general constitutional defect; moreover, this lesion is seldom confined to the kidneys, but nearly always involves the liver, spleen, and gastro-intestinal tract. Amyloid, or, as it is sometimes termed, waxy degeneration, is essentially the outgrowth of a cachectic condition of the system, and most often follows in the wake of syphilis, chronic suppurative processes, such as abscesses, extensive ulcerations, or necrosis. Tuberculosis is frequently traceable in the family history of these cases.

The changes in the kidneys in amyloid disease are very marked, and give rise to a very pronounced train of symptoms; the latter, upon superficial examination, might be mistaken for those of chronic diffuse nephritis. Both the lesions and symptoms, however, are essentially and widely different in character. The author desires to emphasize in the strongest possible manner the importance, therefore, of carefully distinguishing these two renal lesions, since over and over again he has been a witness to the melancholy results of such error. Repeatedly have these cachectic, ill-nourished subjects come under his observation in the last stages of the disease, who had long been consigned to the starvation process of a "milk diet," under the impression that their albuminuria was the result of nephritis.

The Urine.—The characteristic features of the urine in typical amyloid lesions of the kidneys are concisely as follow: The volume of urine is above normal, the color lighter than usual; the transparency is unchanged, the specific gravity is low, albumin is present in marked quantity, and the sediment is very slight in quantity, containing little or no cellular elements; and but a moderate number of casts are present, most of which are of medium size and broad, hyaline orders.

Before considering more minutely these features of the urine it may be premised that the characters of the urine in this lesion of the kidney are exceedingly apt to fluctuate rather widely in different cases; but, notwithstanding this fact, well-marked diagnostic characteristics are not difficult to trace throughout the progress of the disease in most if not, indeed, in all cases.

The quantity of urine in amyloid lesions of the kidneys rules above normal from the beginning, and in most cases the increase is decided. The volume of urine is subject to temporary periods of falling off, and at such periods it may fall below the normal standard. These periods of temporary reduction in the volume of urine may often be accompanied by corresponding attacks of diarrhœa. The specific gravity of the urine is pretty uniformly reduced in marked cases, ranging from 1008 to 1014. Sometimes, however, even in cases attended by a marked degree of albuminuria, the specific gravity ranges as high as 1016 to 1018, and in such cases the prognosis is more favorable. In fact, the few cases of ultimate recovery from this disease observed by the author have, without exception, been cases attended by a comparatively high range of specific gravity of the urine. Cases, on the other hand, are not infrequently met with in which the specific gravity of the urine sinks remarkably low, perhaps lower than in any other form of renal lesion,—1006 and even 1004. Such features are, however, only met with in very late stages, and are usually associated with marked polyuria.

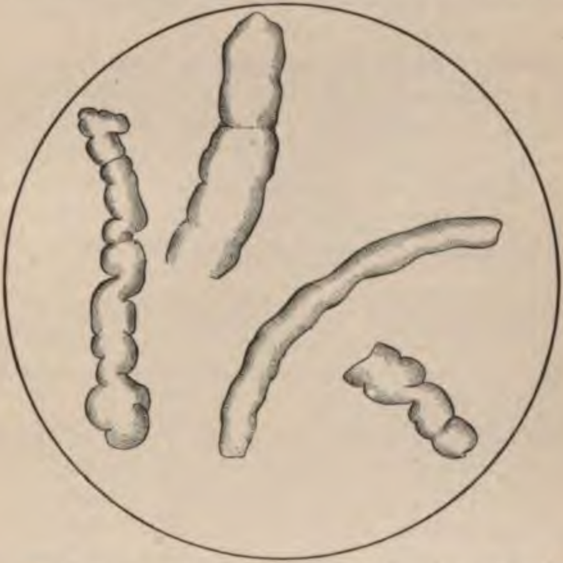

FIG. 42.—WAXY CASTS IN URINE OF AMYLOID DISEASE OF THE KIDNEY. (After Peyer.)

The presence of albumin in the urine may be regarded as an essential feature of amyloid lesions of the kidneys. The urine not only always contains albumin in this lesion, but the albumin is present in considerable, often in large, amount. The usual range is about 4 to 7 grammes per litre (Esbach's method), though it is not uncommon for it to rise to double that amount. The course of albuminuria in amyloid lesions of the kidney is quite variable as to quantity; in the early stages it may be slight, though subject to sudden increase, and with the advent of polyuria may again fall off. The urine always contains globulin in this lesion, often in larger quantity than that of serum-albumin.

Some reduction of the urinary solids is usually to be noted in this lesion. The urea is slightly below the normal standard, probably due chiefly to the lowered state of general nutrition, rather than to the influence of the lesions over the function of the kidneys, since uræmia is rare in uncomplicated amyloid kidneys.

The casts are subject to some variation in number and variety. With the polyuria the casts are often very scarce and almost exclusively of the hyaline order. On the other hand, when casts are comparatively numerous, so-called waxy, yellowish, refracting casts may be present, and occasionally dark, granular ones. The chief distinctive feature about most of the renal casts met with in this lesion is their comparatively large size and hyaline character.

The urinary sediment is comparatively small in quantity in this lesion, in fact unnoticeable, as a rule, to the naked eye, and it is practically devoid of cellular elements throughout if the disease remain uncomplicated.

Leading Clinical Features.—Amyloid lesions of the kidneys appear in the wake of the so-called wasting diseases, or are often preceded by syphilis or some exhausting suppurative process. These patients appear unhealthy and plainly cachectic, except in a few syphilitic cases. The skin assumes a sallow or bronze-like tint, the tongue is nearly always heavily coated, dyspepsia is prominent, and diarrhœal attacks are common. Dropsy is present in most cases, but exceptionally it may be absent until late. Uræmia is exceedingly rare. The liver and spleen become enlarged some time during the course of the disease in the majority of cases. These patients are weakly, anæmic, and enfeebled, with small, thready pulse and cold extremities; but the predominant features throughout are the disorders of the stomach and bowels; dyspepsia or diarrhœa or both demand almost constant attention as the disease becomes advanced.

The distinction between amyloid disease of the kidneys and chronic diffuse nephritis hinges upon the following points: In nephritis the urinary sediment is large in quantity, and contains a large number of casts, including epithelial, dark granular, and fatty casts, as well as those with fragmentary cellular elements attached. Leucocytes, cellular elements, and granular *débris* are prominent features of the sediment. Dyspepsia and diarrhœa are not especially prominent features, nor is cachexia a common accompaniment. The liver and spleen are not enlarged, but anæmia is very pronounced. In amyloid disease the reverse of the above features prevail.

CYSTIC DISEASE OF THE KIDNEY.

This disease is met with in two forms: (*a*) As a congenital obstructive disease, usually associated with absence of the ureter, or other malformation interfering with escape of urine. (*b*) As a disease of adult life, and independent of the congenital form; and in many of its features allied to chronic interstitial nephritis, —indeed, by some authors considered a form of the latter.

Practically, the latter form only possesses a clinical interest to physicians, and to this form the following considerations apply:—

It is not uncommon to find cysts of considerable size in chronic contracting kidney as the result of distal constriction of the uriniferous tubes, which result in proximate dilatation by the urine. In the disease under consideration, however, the cystic formation, though undoubtedly the same in origin (tubular dilatations), yet it so greatly exceeds all other changes in the kidney that the organ increases in bulk sufficiently to entitle it to rank among abdominal tumors. The shape of the kidney is, in the main, retained, and the weight of the organ may reach from 2 to 16 pounds. The disease is almost uniformly bilateral. Dickinson noted but 1 case out of 26 in which the disease was confined to one kidney. Both the medulla and cortex of the organ are replaced by cysts varying in size from a pin-point to the size of grapes or walnuts, the larger ones being usually in the centre of the organ. They contain fluids which vary in color, some being pale straw-colored, deep-yellowish, purple, or bloody. In consistence the contents of the cysts may be serous, viscid, syrupy, caseous or almost solid, consisting of fat molecules, epithelium, crystals of cholesterin, uric acid, and triple phosphates. The cysts do not intercommunicate or terminate with the large conducting tubes, calyces, or renal pelvis, but are essentially closed cavities.

The Urine.—This somewhat resembles the urine in chronic interstitial nephritis. In typical cases the urine is albuminous, the quantity of albumin varying from 5 to 30 per cent. bulk measure. The urine is pale in color when free from blood; of low specific gravity, varying from 1010 to 1015, though it has been noted as low as 1005. Renal casts are usually found, nearly always of the granular order and large size. The urine contains blood at intervals, and sometimes in large quantities. In one of the author's cases the hæmaturia was so severe and persistent for months that the patient became blanched and anæmic to an extreme degree, notwithstanding absolute rest in bed and the use of styptics.

Hæmaturia largely contributes toward exhaustion in many of these cases. In most cases pus is present in the urine in moderate amount. The quantity of urea is markedly reduced, both relatively and absolutely. The phosphates are sometimes increased in quantity, which is rarely the case in interstitial nephritis. The chlorides and sulphates suffer but little change. Triple-phosphate crystals are frequently noted in the sediment, notably in late stages of the lesion, when, as is usual, more or less cystitis is present.

Clinical Features.—The most prominent clinical features of the disease, aside from the urine, are enlargement of the left ventricle of the heart, without valvular disease, and increased arterial tension, as shown by the sphygmograph. The skin is pale and sallow, and cachexia is apparent. The patients are always adults, mostly between the ages of 45 and 60 years. Hæmaturia is prominent, recurrent, obstinate in character, and often profuse. There is usually tumor in renal region; bilateral, though often unequal in size; soft, but non-fluctuant, and preserving the shape of the kidney. In late stages of the lesion there is nausea, vomiting, headaches, suppression of the urine, coma or convulsions, the latter being the most frequent cause of death. Less frequently death results from exhaustion (through renal hæmorrhage), bronchitis, pneumonia, or pulmonary œdema attended by severe dyspnœa.

Cystic disease of the kidney is distinguished from chronic interstitial nephritis by the non-fluctuant swelling in the sides, the recurrent and often severe hæmaturia, and the sallow, cachectic appearance of the patient. From cancer it is distinguished by the absence of pain and slower progress in cystic disease. In cancer there is rapid growth of the tumor, which is of nodular outline and unequal resistance. The age, in cancer, is either under 5 years or over 60, while in cystic kidney the most common age is from 40 to 55. Finally, the aspirating needle will determine if the tumor be cystic or of solid growth.

SECTION X.

DISEASES OF THE URINARY ORGANS, AND URINARY DISORDERS (*Continued*).

RENAL TUBERCULOSIS.

IN the light of recent facts and investigations, tuberculosis of the genito-urinary tract, through hetero-infection, must be considered rare, if indeed possible. Certainly, so far as the kidneys are concerned, it seems out of the question. While careless or unclean catheterization may cause infection of the prostate, involving the vesicula and extending to the epididymis, the anatomy of the urethra and the fact that tubercle bacilli do not multiply in the urine or possess in themselves any degree of motor power negative the view heretofore held by some, that infection may occur through coitus, or the infection reach the kidneys or upper urinary tract through the urine.

Tuberculosis of the kidney occurs in two distinct forms: (*a*) *acute miliary tuberculosis* and (*b*) *local caseating tuberculosis* or "*scrofulous kidney*." The miliary form is mostly met with in children under 10 years of age. It is pretty uniformly bilateral, although the organs often differ in degree of infiltration.

The caseating or scrofulous kidney is most frequent in young and middle adult life, although it may be met with late in life, and it is rare under 10 years of age. Scrofulous kidney is nearly as often unilateral as it is bilateral. Of the two forms of renal tuberculosis the miliary form is about twice as frequently met with as is the caseating or scrofulous kidney. Miliary tuberculosis is always associated with tuberculosis in other parts of the organism, most often phthisis pulmonalis, tubercular meningitis, and tabes mesenterica. This form rarely gives rise to distinctive symptoms, being merged for the most part into general tuberculosis, and, therefore, scrofulous kidney only deserves special consideration in this connection.

Chronic localized tuberculosis of the kidney, renal phthisis, tubercular pyelitis, tuberculous pyelonephritis, or scrofulous kidney, as it is severally known, begins usually at the papillary apices, in the calyces, or renal pelvis, and from thence by the blood- and lymph-channels it extends to the kidney proper. Deposits of cheesy matter infiltrate the renal papillæ, and in the course of a few weeks these form irregular, softened areas, which by progressive infiltration spread deeply inward, involving the parenchyma of the kidney. The organ becomes, in consequence, enlarged and lobulated. The renal pelvis and ureter, on the other hand, become contracted in consequence of thickening of the mucosa, and later on the ureter often becomes choked or blocked by softened and caseous masses detached from ulcerated caseating surfaces above. At the same time the tubercular nodules within the kidney, after reaching considerable size, undergo necrotic changes and break down, forming irregular, rudely-globular cavities. These, as they enlarge, become pyriform in shape and extend until they coalesce, and at length the whole medulla and most of the cortex become involved. The destructive process continuing, the contents of the renal cavities at length burst into the renal pelvis and the whole organ becomes practically an abscess-cavity. If the ureter be pervious the urine washes down the *débris*, which present characteristics soon to be considered in detail. Should the ureter, however, become permanently blocked, dilatation and sacculation of the kidney result,—practically a tubercular pyonephrosis. In case one kidney remain uninvolved the diseased organ either becomes an hydronephrotic cyst or a shrunken, "putty-like" mass; in both cases little, if any, of the secreting tissue proper can ultimately be found. The disease is usually a chronic one in character, and during its course neighboring organs are often involved by direct extension through the capsule of the kidney, more especially the liver and spleen.

The Urine.—Polyuria from tubercular irritation is probably the earliest urinary change. The quantity of urine is increased and the calls to micturate are more frequent than normal. Traces of albumin and a few blood-corpuscles are usually to be found also before destructive ulceration sets in. The urine is usually pale and murky in appearance, of somewhat lowered specific gravity, and of acid reaction.

When ulcerative changes set in the urine presents the following changes more or less marked, according to the degree of degeneration in progress. The urine is of a pale, milky color, the transparency is diminished, the specific gravity is below normal, and the reaction is, as a rule, alkaline. The urine contains pus in gradually-increasing quantity. The pus is less variable in quantity from day to day (unless the ureter becomes blocked) than in most other forms of pyuria. The pus imparts to the urine a more or less pronounced milky appearance, which does not completely subside as in most other conditions of pyuria, but much of the pus remains in suspension even after long standing; this is very significant of renal tuberculosis. The urine contains blood in rather more than 25 per cent. of the cases. If the blood come from the renal pelvis it is usually small in quantity, often unappreciable to the naked eye. Sometimes very marked hæmaturia occurs, usually at intervals; and this denotes ulcerative changes within the renal parenchyma. As the disease becomes advanced the urine usually becomes ammoniacal and markedly offensive, contains ropy mucus, and deposits triple phosphates, small caseous masses, and renal *dêbris.* The urine is albuminous, sometimes highly so; always in excess of the ratio, due to contained pus and blood.

The bacillus tuberculosis of Koch is present in the urine in most cases after necrotic changes set in, and its discovery is diagnostic. The tubercle bacillus can often be demonstrated in the urine by the methods already considered, though this is by no means so easy as in the sputum, owing to the fact that they are relatively few and scattered in the average sample of urine. It is safer, therefore, when suspected, but not found by direct examination, to resort to cultures in gelatin after the usual manner and the inoculation of animals.

Leading Clinical Features.—The leading clinical features of renal tuberculosis are concisely as follow: Polyuria and dysuria, the latter prominent and progressive. The bladder will not tolerate the urine, and is only free from pain or distress when empty. Pain begins about the middle of the act of micturition and continues to the close, but, as a rule, not after. Some pain is usual in the renal region, accompanied by tenderness upon deep pressure. The evening temperature is usually from 2 to 4 degrees higher than normal, or sometimes periods of fever occur, lasting for several days, followed by periods of remission. These patients suffer from profuse night-sweats, loss of appetite, debility, and emaciation in the course of the lesion; while cough and diarrhœa are scarcely less frequent accompanying features of the disease. Uræmic complications are rare.

From calculus the distinction hinges on the slow development and irregular degree of pyuria, which is usually preceded by slight hæmaturia in calculus. The general nutrition is better preserved than in tuberculosis. The pain on micturition is relieved at the close in tuberculosis, while in stone it is increased. Absence of temperature and constitutional symptoms characterize the progress of calculous disease, while they are prominent in tuberculosis.

RENAL CANCER.

Primary cancer of the kidney may appear in the form of carcinoma, sarcoma, and rarely as lymphadenoma. Sarcoma is most frequently met with in childhood, while carcinoma is mostly met with after 40 years of age, the encephaloid being the most frequent variety of the latter, though occasionally the melanotic growth is met with. Primary cancer usually attacks but one kidney; only exceptionally is it bilateral. Of 59 cases collected by Ebstein, 31 involved the right kidney, 23 the left, and 5 both kidneys. Encephaloid cancer of the kidney sometimes attains an enormous size,—14 to 56 pounds.

Renal cancer is more frequent in males than in females. Though slow of development, often remaining quiescent for years, when once it has begun it rapidly progresses toward a fatal termination,—usually within a year or two. The disease begins in the fibrous stroma of the cortex or in the tubular epithelium; sometimes, however, primary invasion begins in the lymphatics about the hilum. Wherever the primary lesion begins, the whole organ eventually becomes infiltrated. There is usually appreciable tumor after the disease becomes thorougly established.

The Urine.—The most prominent feature of the urine in cancer is hæmaturia. In carcinoma this is especially pronounced, often recurring and frequently uncontrollable. In the other forms of cancer hæmaturia may sometimes be absent throughout. Hæmaturia is variable, occurring sometimes early, and subsiding as the disease progresses, when it may disappear and not return. Again, the disease may become advanced before blood appears in the urine. As a rule, when palpable tumor is present there is hæmaturia. The hæmaturia is somewhat characteristic in its irregular intermittency, appearing and disappearing at intervals without apparent cause; while often profuse, it is yet rarely so excessive as to rapidly produce anæmia or exhaustion. Albumin is usually present in the urine in small quantity; always present if there be blood. The quantity of urine is usually increased unless the ureters become blocked by blood-clots. Pus is present but in small quantity, save in advanced cases, attended by decided destructive changes in the kidney; and even then the quantity of pus is remarkably small in amount, considering the extent of necrotic changes in progress.

In carcinoma the urine frequently contains acetone, even before there is advanced emaciation. Frequent micturition is the rule, and it may be so pronounced as to call attention chiefly to the bladder when only the kidney is involved. The presence of organized substances in the urine, such as epithelium, casts, etc., are of little diagnostic value in renal cancer. Cancer-cells are not recognizable in the urine in this disease, and those alleged to have been found were doubtless transitional epithelium, which is often present in considerable quantity if malignant disease invade the renal pelvis. The only significant feature in this connection would be the discovery of particles of the morbid growth with distinct alveolar structure in the urine, but in malignant disease limited to the parenchyma of the kidney this is practically unknown.

Leading Clinical Features.—Increasing tumor is the almost invariable rule, which is to be looked for in the anterior lumbar region, between the costal arch and the crest of the ilium. If large the tumor approaches the umbilicus, extending upward and downward into hypochondrium and iliac, and even to the inguinal regions. The tumor is usually lobulated or presents obtuse margins; the lobulations often possess unequal degrees of hardness.

The tumor is nearly always fixed. Pain occurs early, usually persistent in character, though sometimes intermittent. It is most severe in the affected kidney, but may be reflected to neighboring parts. The character of the pain is dull and aching, often paroxysmally increased, but not greatly aggravated by body movements. At first the pain is usually slight or even vague, and at times absent, becoming again severe and prolonged. From dull in the beginning it may later on become lancinating, either spontaneously or evoked by pressure, but not by movements. When tumor becomes large and presses upon the larger trunk-nerves, pain often extends to the chest, across median line, and downward to the hips and limbs, simulating sciatica. The pressure exerted by tumor when the latter is large often causes œdema of the feet and legs, ascites, and prominence of the superficial abdominal veins, as well as constipation, disturbances of the stomach, and icterus. The constitutional symptoms include emaciation, anæmia, cachectic appearance,—browning or sallowing of the skin,—failure of strength and vitality. Uræmia is rarely, if ever, present, unless nephritis co-exist. Accidental or complicating features are sometimes added; such as paraplegia from spinal pressure, vesical paralysis with retention of urine, asthmatic or laryngeal dyspnœa, and spasmodic cough from extension of the pathological process.

Differential Features.—From hepatic tumors cancer of the kidney differs as follows: The former have no intestine in front of them; the dullness upon percussion is uniform throughout. Renal tumors lie in part behind ascending colon, which passes obliquely up and to the left, giving clear note of percussion on lower and inner margin. *Splenic enlargement* presents rigid, thin borders instead of round and lobulated ones, and, moreover, as a rule, splenic tumor has more mobility, and deep percussion often elicits intestinal resonance through its substance. There is usually antecedent history of ague or intermittent fever, leucocythæmia, etc., in splenic enlargement.

Renal Calculus.

Calculi may originate in the secreting structure of the kidney—usually in the tubules—or in the renal calyx, but their development is most common within the renal pelvis; although this sometimes takes place in the infundibula, calyces, or even in the dilated tubules, which form cavities for their location in the parenchyma of the organ.

Renal calculus is usually unilateral, though many exceptions occur to this general rule. The calculus when large is usually single, the smaller ones being more apt to be multiple.

Renal calculus occurs at all ages, including intra-uterine life. It is, however, most common before 15 and after 50 years of age. In young people and children calculus is most frequent among the poor, while calculus in advancing life is most common in people of comfortable circumstances and luxuriant habits. As a rule, the calculi in infancy is of the ammonium-urate variety; that in young adults, uric acid; that after 40 years of age is usually calcium oxalate.

The Urine.—Blood appears in the urine in the vast majority of cases of renal calculus, and presents the following features: Hæmaturine not profuse, but appears in repeated paroxysms; *increased by exercise.* The blood is intimately mingled with the urine; is not bright in color, but smoky-brownish or porter-colored. The volume of the urine is not increased in uncomplicated renal calculus, but is rather diminished. The urine is usually sharply acid and of high color. The above are usually the early features of the disease, before pyelitis begins. After pyelitis is established the urine undergoes the following changes: Pus and mucus appear in the urine in greater or less quantities. More or less frequency of micturition is present, and the act is accompanied by uneasiness,—sometimes amounting to pain. This may be so pronounced as to lead to an impression that cystitis exists. The deposits in the urine are significant, but care should be taken to secure only primary deposits,—not those due to decomposition changes. Centrifugal sedimentation of the urine is the only trustworthy method of securing this. Urates and oxalates are often observed in the sediment, the former frequently in quantity. With the advent of pyelitis, more or less phosphatic deposit is to be found in the urine. Epithelium in greater or less quantity is found in the sediment in advanced renal calculus, most often the angular and spindle form. Lastly, the appearance of small-sized concretions in the urine often furnish diagnostic data of the highest value.

Leading Clinical Features.—These consist of dull aching pain situated deeply in the loin, usually unilateral, and often radiating along the ureter toward the testicle, down the thigh, and sometimes extending as far as the foot. The pain may be sharp and lancinating at times; intensely severe paroxysms are occasional features (renal colic), lasting a few hours and then suddenly subsiding. The ordinary pain of renal calculus is invariably increased by exercise, either walking or riding; it is, therefore, more marked in the evening than in the morning. Tenderness upon deep pressure anteriorly is to be found, especially if the calculus has excited inflammation.. Gastric disturbances are common, including nausea, vomiting, and periods of more or less disorder of digestion,—acidity, flatulence, etc.

Differential Features.—The early stages of renal tuberculosis are most likely to be confounded with renal calculus. In renal tuberculosis there is usually tuberculous history in the family, and often tuberculosis may be found elsewhere in the patient, as in the joints and glands, and the age is usually from 20 to 40. Polyuria is not prominent, and renal colic is rare save late, and then less severe, usually not causing retraction of the testicle. Hæmaturia is more persistent, but not so much influenced by movements or exercise. The urine is cloudy from the beginning, of low specific gravity, depositing more pus, and albuminuria is early and more pronounced. Tubercle bacilli usually are present in the urine, and inoculation of animals with urine deposit induces tuberculosis. General symptoms are prominent, such as anæmia, emaciation, weakness, rapid pulse, and evening temperature, with night-sweats. These features are, for the most part, absent in stone.

From malignant disease the distinction rests upon the more decided hæmaturia of the former, which often results in anæmia. Hæmorrhage is uninfluenced by movement, and therefore it occurs at night as well as by day.

RENAL EMBOLISM.

Renal embolism consists of an impacted thrombus which has formed in some part of the circulatory system,—usually in the heart,—and is carried by the blood-current to the kidney, where it blocks one of the renal vessels. Recent endocarditis furnishes the most frequent source of renal embolism. As the fibrinous clots accumulate upon the cardiac valves, sooner or later they become detached in whole or in part, and those from the left side of the heart are liable to be carried by the blood-current into either kidney. The anatomical results of embolism are very constant and striking, and in few organs are they more often noticed at the autopsy than in the kidneys, though they are not so frequently recognized during life as in some other locations, notably in the lungs or brain.

The Urine.—Changes in the urine are very striking in renal embolism, although they are not wide-spread. Sudden and pronounced albuminuria is almost invariable. Albumin may appear in the urine in a few hours after the attack, but sometimes not for twenty-four hours or so after impaction. The albuminuria is marked in degree for from two to five days; it then gradually diminishes and completely disappears, or leaves only mere traces after two, three, or four weeks. The specific gravity of the urine is decidedly increased in the beginning, often reaching 1030 to 1035; it gradually lowers from day to day, and the normal range is reached after a few days or weeks. The quantity of urine is decidedly diminished at first, the color is dark brown, and the reaction is sharply acid. Blood is usually present from the beginning in variable, but rarely excessive quantity. Some degree of pyuria is to be noted, but this is rarely pronounced.

The urine contains casts in this lesion, often in considerable numbers. At first they are mostly hyaline; later on epithelial casts appear, as well as those with pus-corpuscles attached to them. After the first five to seven days the casts become less numerous, they are mostly hyaline, and at length they disappear from the urine. It will be seen from the above features that the urinary changes begin abruptly, but that the urine progressively and steadily resumes its normal characteristics, and, in from a few days to three or four weeks, all manifestations of urinary disturbance pass away. The block, if aseptic, remains in the kidney, but ceases to become a source of renal irritation.

Leading Clinical Features.—A previous history of endocarditis is the rule. The impaction is followed at once by sudden pain in the renal region, often accompanied by chills, which latter may be repeated, and some irregular action of the heart, with sense of præcordial oppression, or clogging, and frequently dyspnœa. Some slight elevation of temperature is usual. If the pain be very severe vomiting is usual, and even some degree of collapse may follow.

URÆMIA.

The intimate toxic character of uræmia as yet remains an unsolved problem, only known to us by its results. Our knowledge of this matter, therefore, is inexact as yet, and remains for the chemico-physiologist to unravel. In the light of our present knowledge of this subject, the only conclusions that seem justifiable are as follow: (*a*) All theories attempting to explain the cause of uræmia through the action of any single product or toxin must be abandoned as fallacious, as the toxin is undoubtedly multiple. (*b*) The general cause of uræmia lies in the failure of the kidneys to excrete the urine in part or in whole, and that the urine or its primary elements, as retention products, act as direct toxins upon the organism, evoking the symptoms termed uræmic. (*c*) That the most successful attempt at isolation of these products of the urine to date we owe to the investigations of Bouchard. (See Section V, page 143.)

Uræmia may appear as an acute and rapidly overwhelming toxicosis, causing coma, convulsions, and death within a few hours; or it may linger for weeks or for months as a milder form of toxic disturbance, with symptoms such as somnolence, restlessness, headaches, nausea, attacks of diarrhœa, dyspnœa, visual disorders, and general disturbance of nutrition.

The Urine.—This furnishes the key to the diagnosis of uræmia with great uniformity. The essential feature of the urine in uræmia is diminution of the absolute amount of solids, but more especially of urea. The quantity of urea excreted, instead of being 500 grains for an average body-weight, becomes reduced to 200 or 100, and even less than 50 grains in some cases. As a rule the activity of the symptoms bear an inverse ratio to the quantity of urea excreted, and therefore, in those cases attended by extreme diminution of the excretion of urea, the symptoms are sure to be pronounced and threatening so long as this continues. The uric acid, chlorides, phosphates, and sulphates of the urine also suffer marked reduction in uræmia, but, with the exception of uric acid, these are probably of no special significance. As a rule the volume of the urine is diminished, and the degree of diminution varies through all degrees up to complete suppression. The specific gravity of the urine, notwithstanding the decreased volume, is also decreased, and sometimes markedly so, descending frequently to 1008 or below. Exceptions to this rule are noted sometimes in acute diffuse nephritis, when the volume of urine is reduced to a few ounces, the urea being still decreased both relatively and absolutely; but the febrile condition accompanying the acute nephritis causes some increase in the other solids, which proportionally become excessive, and thus raise the specific gravity of the urine sometimes even to the normal range.

With regard to the morbid constituents of the urine in uræmia, albumin is the most constant feature, and is present in all grades, from mere traces up to 2 or 3 per cent. by actual weight, depending upon the nature of the associated lesion. It should be borne in mind, however, that while albumin is usually present in the urine in uræmia, exceptional cases occur in which it is said to be absent; though this is rare. Even in those cases of chronic interstitial nephritis characterized by absence of albumin in the urine, the exciting cause of a uræmic attack, especially if acute, is apt to be of sufficient congestive character to cause, at least, mild albuminuria. It may, therefore, be repeated that active uræmia is *extremely rare* without accompanying albuminuria.

The urinary sediment in uræmia includes a very wide range of morbid products with no very constant associated features. We may have casts, epithelium, pus, blood, bacteria, together with crystalline or amorphous deposits of urates, phosphates, oxalates, etc. The only products that may be considered at all constant are renal casts, which are rarely—perhaps never—absent in uræmia. Sometimes they are extremely sparse and may be overlooked without due care; notably so in chronic interstital lesions of the kidney, in which their form is often limited to the small, perfectly-clear, non-refracting variety of casts, which are confessedly difficult to find; but failure to find them does not, without every precaution, prove their absence. With our improved methods casts should be found when present. The nature and number of renal casts will depend upon, and correspond to, the character of the renal lesion present, which need not be repeated here. For full consideration of this subject consult Section VII, page 187.

Corresponding Clinical Features.—Among the milder symptoms of uræmia may be mentioned dyspepsia, flatulence, nausea, occasional diarrhœa, neuralgia or headaches, vertigo, dyspnœa of an asthmatic type, bronchial catarrh, and various nervous disturbances, such as insomnia, restlessness, mental depression, numbness of certain parts of the body, drowsiness, and certain visual disorders.

The more pronounced symptoms include severe headache, usually frontal; vomiting, extreme nervousness, twitching of the muscles, drowsiness; pulse increased to 100 or over, usually hard and tense; temperature lowered unless some inflammatory action be associated; tongue coated with dry, brown fur; breath foul (uræmic), and often more or less profound stupor or coma, or convulsions, or both.

Differential Features.—Uræmic coma may be mistaken for a variety of conditions, notably apoplexy, epilepsy, alcoholic or opium narcosis.

Uræmic coma may be known by the following features: The subjects are usually young or middle-aged; previous attacks are unlikely; renal lesions are present in some form; appearance of the patient is pallid, sometimes cachectic; pulse increased to 100 or over; the pupils tend to dilate; the respirations may or may not be hastened; breathing is stertorous and *labial;* unconsciousness is not complete, the patient may be partly aroused by efforts; a peculiar odor of breath is present (uræmic); the convulsions are of recurrent order, and, as a rule, albuminuria is present.

Apoplexy is differentiated as follows: The age of the patient is nearly always past medium life, often advanced; previous attacks unlikely; heredity marked; granular kidney often associated; appearance of patient normal; pulse slow, full, 60 per minute or under; pupils unequal; respirations slow, stertorous, and *deeply guttural;* insensibility complete and profound; patient cannot be aroused; hemiplegia is present.

Epilepsy is most common under 30 years of age; previous attacks are the rule; the appearance of the patient is dusky, purple, gradually becoming paler; pulse slightly accelerated, small, feeble, and dicrotic; temperature normal, or a degree or so above; pupils normal; respirations stertorous, guttural, unsteady; unconsciousness is not complete, coma of brief duration; great muscular relaxation present.

Alcoholism is common to all adult ages; previous attacks are the rule. The features are suffused and bloated, the lips livid, and the expression vacant; pulse frequent, small, and feeble; temperature slightly lowered, pupils dilated; respirations are deep and slow; stertor is intermittent; breath is alcoholic; vomiting is common; the conjunctivæ are injected; the features are swollen, and the subject can usually be partly aroused.

Opium coma is most frequent in the young, and may be habitual or accidental. The features are shrunken, pallid, cyanotic; expression is ghastly; pulse usually slow and feeble; temperature not increased, rather lowered; pupils contracted; respiration slow, shallow, and feeble, and opium may be detected in the breath.

HÆMOGLOBINURIA.

Hæmoglobinuria constitutes a condition characterized by the escape of the blood coloring elements by way of the urine, very little, if any, of the corpuscular elements of the blood accompanying the pigmentary elements. From whatever general source it may originate, it is primarily due to dissolution of the red corpuscles of the blood, which permits the coloring matters to escape in solution. As an occasional phenomenon it may be met with in the course of certain infectious diseases, extensive burns, and in various forms of poisoning. In addition to this it occurs as an idiopathic disease of intermittent character, and to such the following considerations are intended especially to apply :—

This disease is most common in males,—three or four to one. It occurs at all ages, from 3 to 52 years, but most often between 20 and 50. Malaria seems to be the most prominent historical feature of these patients, while cold is undoubtedly the most frequent exciting cause.

The Urine.—The appearance of the urine in the intervals between the attacks is perfectly normal; but with the attack its appearance becomes at once strikingly altered, apparently bloody. The color assumes a dark-red, port-wine, or porter color, and is somewhat turbid or smoky in appearance, and deposits, upon standing, an abundant chocolate-like sediment. The specific gravity of the urine varies from 1015 to 1030, the average range being slightly above normal,—1023 to 1025. The reaction of the urine may be acid or faintly alkaline, and the volume is somewhat above normal. In most cases the quantity of urea is increased. The urine gives a highly albuminous reaction, and further testing shows the presence of globulin.

The urinary sediment is chiefly made up of amorphous granular matter,—doubtless disorganized blood-corpuscles,—in which are often to be seen minute crystals of hæmatin. Casts are usually present, chiefly dark, granulated ones, though often, also, hyaline casts may be found. Many of the casts are made up of hæmoglobin. Calcium-oxalate crystals are usually present, and less frequently are uric-acid crystals found. Blood-corpuscles are either absent or only a few scattering ones are to be found. The urine gives the characteristic blood reaction with guaiacum and ozonic ether; even the interparoxysmal urine often shows the blue reaction. The spectroscopical examination of the urine shows the two absorption bands between Frauenhofer's *D* and *E* lines characteristic of oxyhæmoglobin. Renal epithelium is often seen in the sediment, sometimes deeply stained by the blood-pigment. Amorphous urates are usually present in abundance, especially as the attack is subsiding. The chlorides of the urine are usually deficient, the phosphates and sulphates in excess, and so-called indican is not infrequently present in considerable excess.

Prominent Clinical Features.—The symptoms of idiopathic hæmoglobinuria are distinctly paroxysmal, beginning with chill, —sometimes continued rigors for an hour or more,—which are usually due to previous exposure to cold. The exposure, however, does not cause the disease, but merely provokes the paroxysm, as is proved by the fact that so long as the patient remains warm he continues free from symptoms. The chill is accompanied or followed by retching and often vomiting, as well as pain in the back and limbs; often with retraction of the testes. General malaise succeeds with yawning and stretching. Sometimes tenderness in the renal region is to be elicited upon deep pressure. Thirst, headache, and drowsiness are frequent features, and the skin sometimes becomes jaundiced. In from half an hour to two hours the patient voids more or less port-wine-colored urine, The urine retains this abnormal color for two or three passages; the whole attack usually being completed in twenty-four hours or less time; more rarely it may continue for several days. The attack is often succeeded by griping pain in the umbilical region. and more or less pallor and weakness succeed the attack for a day or two. Urticaria is an occasional accompaniment of the disease.

The temperature is lowered during the cold stage (96° F.), but often rises above normal when the chills subside. After the attack the patient remains apparently well for a longer or shorter time,—it may be for months,—until again exposed to cold. Nephritis is not an infrequent result; protracted cases are characterized by repeated paroxysms.

CHYLURIA.

This disease usually arises in consequence of some lesion of the lymphatic system, whereby the chyle is diverted from the natural channels into some part of the urinary tract. As an idiopathic disease chyluria has heretofore been almost exclusively confined to the tropics, or to those who have spent much of their lives there. As such it depends upon the invasion of the blood and urinary tract by a parasite,—the *Filaria sanguinis hominis*,—as first pointed out by Dr. Lewis, of Bengal, and already described and illustrated (page 208). Besides the endemic form, the disease is occasionally met with in people who have never lived in the tropics, and, when thus occurring, it may be considered an accidental condition, brought about by traumatisms or diseases which have established communications between the lymph-channels and the urinary passages. The accidental form of the disease is comparatively rare; at least nine-tenths of the cases met with, even in temperate climates, are the result of infection in the tropics of people who previously there resided and contracted the disease.

The endemic form prevails widely in the tropics, including especially India, China, the West Indies,—notably in Barbados, Trinidad, and Demarara,—also Cuba, Bermuda, Brazil, Mauritius, the Isle of Bourbon, and South Australia. The disease attacks indifferently both natives and foreigners, males and females, and shows but little preferences as to age of the subject. The peculiar and interesting nature and habits of the parasite which causes this disease have already been fully described (p. 209).

The Urine.—The peculiar condition of the urine in chyluria furnishes the key to the recognition of the disease. The appearance of the urine is characteristically milky, and it so remains upon standing for days without settling, in consequence of the finely molecular division of the contained fat, thus permitting it to remain in suspension. It is unusual for oil-globules of any size to be found in the urine in this lesion; indeed, the emulsion is so complete that only minute granular matter is seen. Sometimes, upon standing, the fat rises to the surface of the urine and collects in cream-like flakes. The quantity of fat found in the urine in chyluria varies greatly, depending largely upon the quantity and quality of the food taken; the urine of digestion (after food) is richest in fat, while that of fasting contains the least.

If the urine be shaken with ether the fat is dissolved and the urine assumes its normal color and appearance. In addition to fat, chylous urine usually contains blood in sufficient quantity to impart a very noticeable pink color to the fluid. The pink tint is fainter than would be expected in proportion to the quantity of blood actually present, the opacity caused by the fat greatly obscuring the coloration due to the blood-corpuscles. Upon standing, however, the contrast becomes striking; the bright sediment of precipitated blood is then plainly visible. This precipitated blood-clot becomes more pronouncedly pink upon exposure to the atmosphere, as first pointed out by Dr. Vandyke Carter.

A notable characteristic of chylous urine is its tendency to spontaneous coagulation upon standing. If the urine be at all rich in fibrin, shortly after it is voided it will coagulate into a firm, vibrating, jelly-like mass resembling corn-starch *blanc-mange.* Unfortunately, sometimes coagulation takes place in the urinary channels, notably the bladder, and may give rise to most distressing symptoms until it be dissolved or broken up and removed. The clots which form after the urine is voided often become very firm, and long retain the form of the vessel in which the urine stood; if in bottles they may even have to be broken in order to remove the coagulum. The coagulation of chylous urine depends directly upon the fact of the almost constant presence of fibrin in the urine, although the quantity varies considerably. At times it is insufficient to cause coagulation. The quantity of fibrin present is usually in inverse ratio to the amount of contained molecular fat.

The uniform presence of albumin in the urine is attested by the constant coagulation of the urine by heat or other albumin precipitants. Corpuscular elements are sometimes present in the urine, besides red blood-cells resembling lymph-cells, as well as large oval and rounded cells which microscopically and chemically evince the characteristics of epithelium. The urine is usually devoid of renal casts unless nephritis be excited by the disease; and since the urine always contains fibrin, this would indicate that the lesions are not situated in the kidneys, but rather in the conducting channels of the urine. Filaria are sometimes found in the urine, especially of the tropical form of the disease, if sought for in the night urine. In urine excreted during the day they are rarely to be found, owing to the fact that the parasite is quiescent during the day. Pus-cells are more or less numerous in the sediment.

The solids of the urine suffer some reduction owing to the drain upon the elements which go to furnish nutrition. The specific gravity is lowered to a moderate, rarely to an extreme degree,—1016 to 1010. The urea, chlorides, and sulphates are usually deficient, especially the two former, while the phosphates are often considerably increased. It is common to find a considerable deposit of uric-acid crystals in the freshly-voided urine upon cooling.

Leading Clinical Features.—The clinical symptoms are rather negative; dropsy, uræmia, and frequent micturition being absent. There is usually an indefinite dragging pain in the back and loins, especially preceding the attacks. Anæmia becomes more or less marked according to the extent and continuance of the drain. Loss of strength and depression are prominent features during the escape of chyle; these, however, are at once relieved if this cease. Tuberculosis often becomes a complicating feature of very chronic cases. The disease pursues an intermittent course,—especially so the tropical endemic,—due to successive ruptures of lymphatics; the accidental form is more uniform in its course. The duration of the disease is indefinite, but always chronic, lasting from ten to forty-seven years.

Diabetes Insipidus.

This disease has been variously designated under the terms *diuresis*, *polyuria*, *polydipsia*, and *hydruria*. Little or nothing definite is known as to the pathology of the disease; it is not improbable that it is caused by a number of different morbid conditions. The disease is much more frequent in males than in females. It may appear at any age, but in the majority of cases the disease appears between 5 and 30 years of age. From the number of alleged causes of the disease by various authors, it is very evident that nothing definite is known of the etiology, save in those cases that can be distinctly traced to traumatisms, intracranial growths, or other lesions of the nervous system.

The Urine.—The chief features of the urine are: enormous increase of volume, lowered specific gravity, and absence of both sugar and albumin. The daily volume of urine not infrequently reaches from 15 to 40 pints. The urine is pale in color, almost, in fact, watery in appearance, and the specific gravity ranges from 1002 or 1003 to 1007. The reaction is feebly acid or neutral. Upon standing, the urine soon becomes ammoniacal and turbid from precipitation of earthy phosphates, and gives a rather offensive, fish-like odor. The urea, while proportionately reduced, is, in fact, absolutely increased considerably above the normal range. Uric acid is apparently greatly deficient, and it is even claimed to be often absent. The increase of urea and deficiency of uric acid favor the presumption that the latter undergoes conversion into the former. The chlorides, phosphates, and sulphates are more or less increased, more especially the phosphates, which sometimes become greatly excessive. Albumin is usually absent from the urine, although in protracted cases it is often present in small quantities. Inosite is frequently present in the urine, as Strauss claims, merely as the result of irrigation of the tissues, since he succeeded in producing the same condition, experimentally, upon subjects by administering copious draughts of water.

Prominent Clinical Features.—The most prominent symptoms of this disease are as follow: Inordinate, constantly-recurring thirst, which is only briefly quenched by copious draughts of water. Less constantly the appetite is increased. These patients are sensitive to cold and are easily chilled, the temperature being somewhat lowered. The tongue is dry, and more or less discomfort is experienced in the stomach; pain and diarrhœa are often present. The skin is dry, pinched, and dusky. The patient becomes spare and weak, though, exceptionally, fair strength and health is maintained for years. In late stages of the disease, œdema of the lower extremities sometimes appears.

Diabetes Mellitus.

Saccharine diabetes constitutes a perverted state of the elaborative functions in which certain elements which go to make up nutrition—notably starches and sugars—fail to reach their normal destinations in the economy. The symptoms evoked are partly due to lack of nutrition and partly to the damaging effects of the waste products (chiefly sugar) upon the tissues. The direct cause of the disease is an impaired functional capacity of the liver in its glycogenic relations. This may, however, be induced through impaired nervous influences, which may be central or reflected. In addition, some complemental relationship exists between the functions of the liver and pancreas, which often permits lesions of the latter organ to evoke the phenomena of diabetes mellitus. The precise nature of this relationship is unknown.

Something over 30 per cent. of the cases can be traced hereditarily. The disease is notably frequent among Hebrews. It attacks males twice more frequently than females. It occurs most often between the ages of 25 to 65, and is infrequent at the two extremes of life. In young people under 30 years of age the disease is almost uniformly progressive toward a fatal issue in from a few months to four or five years. If the disease do not appear until between 40 and 50 years of age, it is often more amenable to treatment; after 50 it may usually be held in control by proper management. The disease is more severe in spare than in stout subjects, at all ages. In the young death is most frequent from diabetic coma, while in those advanced in life the end is often reached through cardiac degeneration, gangrene, or exhaustion.

The Urine.—The physical characters of the urine are characteristically altered in typical saccharine diabetes. The urine is light in color and of a greenish, rather than yellowish, tint. It remains perfectly transparent and froths much if poured from one vessel into another. The specific gravity is markedly increased, ranging from 1030 to 1045, or even higher. The reaction is sharply acid, and it long remains so upon standing. The quantity of urine is greatly increased, the increase being usually in direct ratio to the quantity of contained sugar. From 6 to 12 pints of urine are often voided in twenty-four hours, but in severe cases 25 to 40 pints are sometimes excreted.

The most characteristic feature of the urine is the presence of sugar, which forms the index to the disease. The quantity of sugar varies from 1 to 8 per cent., averaging perhaps 4 or 5 per cent. One and a half to two pounds of sugar per day constitute the highest range of sugar excreted in the more extreme cases, while half a pound is not uncommonly excreted in ordinary cases. The quantity of urea is markedly increased. A marked decrease in the quantity of urea may be considered as an unfavorable indication. The uric acid is usually deficient, often reaching but half the normal amount or even less. Notwithstanding the above fact, uric-acid crystals are frequently deposited from freshly-voided diabetic urine; the deficiency of coloring matters and disproportion of salines permitting it to fall out of solution. The sulphates of the urine are not materially altered in quantity, probably because of the large amount of animal food usually eaten in these cases. The gross chlorides, like the sulphates, remain essentially unaltered in quantity, though often varying considerably from day to day. The phosphates vary greatly according to the quantity and quality of food taken, but, on the whole, the tendency is toward increase.

The urine often contains, in the advanced stages, acetone or an acetone-yielding substance. Diacetone is occasionally present in the urine, but only in serious cases, and it is usually the index of approaching *diabetic coma.* Albumin is often present in small quantity in chronic cases. It may be due to co-existing nephritis, but more often to disturbance of the renal circulation, impaired nutrition of the renal epithelium, or degeneration of the parenchyma of the kidneys.

Prominent Clinical Features.—The most prominent symptoms are: thirst, polyuria, lowered temperature, hunger, weakness, emaciation, and nervous disorders. The thirst is constant, and seemingly unquenchable in character. Although the amount of water consumed is sometimes enormous, the mouth and throat remain dry and parched. The appetite is always increased, at first sometimes inordinate, and but little appeased by food. As a result the stomach sooner or later becomes disordered under the strain of constant overloading, so that in late stages of the disease the appetite fails, and dyspepsia follows. Constipation and attacks of diarrhœa are common. The mouth, tongue, and fauces become intensely red and congested; the gums become tender and shrunken so that the teeth sometimes loosen. The temperature is lowered,—96° to 97° F. being common, but even a temperature of 93° F. has been observed. Chilly sensations are frequent; so that these patients instinctively seek the fire and require extra clothing. Colds are excited upon slight exposures.

Periods of somnolence are common, and various nervous manifestations appear, as neuralgia, cutaneous hyperæsthesia, sensations of abnormal heat of skin, sudden spells of perspiration. These patients become irritable, fretful, uneasy, vascillating, and the mind deteriorates somewhat. The sexual power declines or is completely lost. The skin is dry, harsh, unperspirable, wrinkled, and loose, causing an early aged appearance. Emaciation progresses sometimes with rapidity; the muscles feel weak and tired, so that movements become laborious and exhausting,—these patients do not care to exercise. The pronounced and persistent polyuria produces frequent micturition, which harasses the patient both day and night. Tuberculosis sometimes sets in in the late stages of the disease, often, however, preceded by bronchitis or localized pneumonia. Gangrene of the extremities is common in aged subjects. Cardiac enlargement, high-tension pulse, and degenerative changes of the heart often supervene in long-standing cases.

Finally, gastric pain, dyspnœa, and more or less drowsiness announce the approach of *diabetic coma*, which quickly terminates life.

URINARY FEVER.

Various names have been applied to this disease, such as *urethral fever*, *catheter fever*, *urinary fever*, *shock*, *urinary poisoning*, *uræmic poisoning*, *urinary infection*,—names which suggest the various and conflicting views held both of the etiology and pathology of this condition, which, indeed, still remain unharmonized.

The term "urinary fever" was first employed by Guyon to denote the febrile disturbance and accompanying phenomena set up by instrumentation of the urethra or bladder, or by operations upon the urinary organs, or by impressions upon the urethra or bladder by other means. The morbid phenomena evoked by instrumentation of the urethra and bladder may become so wide-spread as to include septic inflammations of the renal pelvis, the kidney itself, and even pyæmia; or it may bring about acute uræmia, with its attendant consequences, often terminating in death. In most of these conditions some previous disease existed either in the kidneys, bladder, or urethra, and the instrumentation merely served to convert a chronic disease into an acute and often highly-dangerous condition. Much of the confusion in the past, and, to some extent, still existing, in reference to the pathology of urinary fever, has arisen from the mistake of describing the various inflammatory and septic processes set up in abnormal urinary organs by instrumentation, and attempting to harmonize these with the temporary fever induced by instrumentation of the urethra and bladder. We may, for instance, have all the conditions present which tend toward the development of septic nephritis, such as obstructive cystitis or ascending pyelitis. The use of the catheter under such circumstances, especially in elderly men, is very apt to at once evoke acute (septic) interstitial nephritis, resulting in death. While the exciting cause in such case was instrumentation, pathological conditions pre-existed, and the instrumentation merely served to convert a chronic into an acute septic disease.

By urinary fever, as here considered, is meant the elevation of temperature and accompanying symptoms evoked by the passage of a sound or catheter, by operations or other impressions made upon the lower urinary tract, *the kidneys and urinary organs being free from disease.*

The passage of a catheter into a healthy urethra, when the bladder and kidneys are perfectly healthy, may evoke symptoms and results of all grades, from a mere transient faintness, recovered from in a few minutes, to violent chill, elevated temperature (103° to 105° F.), suppression of urine, convulsions, and even death in from six to forty-eight hours. Morris has especially pointed out that the nervous connections with the genito-urinary tract are so peculiarly constituted that, if a local irritation be at all pronounced, conditions are favorable for the most wide-spread nervous storm to prevail over the entire sympathetic and cerebro-spinal systems, involving the cardiac, pulmonary, and renal circulations to the extent of inducing syncope, impaired respiration, acute renal congestion, convulsions, and even death.

But even the slighter forms of local irritation (measured by the degree of instrumentation), as the gentle passage of a sound, are as likely to evoke an attack of urinary fever as operations upon the urinary organs of very considerable extent, such as lithotomy or lithotrity.

The Urine.—The quantity of urine is more or less diminished in urinary fever. The diminution is usually very decided and even complete suppression may occur, lasting for one to three days. Very decided diminution is the rule; complete suppression rather the exception. In cases of recurrent urinary fever unattended by suppression the volume of urine is much diminished during the febrile period, while during the intervals the volume increases considerably. The color of the urine is increased and often presents a bloody tint. The urine is smoky in appearance, the transparency being more or less diminished or absent. The reaction of the urine is acid and the specific gravity reduced. The solids are diminished, notably the urea. Blood is nearly always present in marked cases, varying from microscopical quantities to frank hæmaturia. Albumin is constantly to be found in the urine; the range, however, is usually moderate,—one to two grammes per litre,—although exceptionally two or three times that amount is present, and this is always of grave significance. Casts may or may not be present. They are always associated with high grades of albuminuria, and, like the latter, are of serious significance.

Prominent Clinical Features.—After passing a catheter, or some operative manipulation of the lower urinary tract, in from a few minutes to six or eight hours the patient is suddenly seized by a chill of various degrees of severity, from merely chilly sensations to pronounced and violent rigor, accompanied by chattering of the teeth and vibrations of the limbs or whole body. This is followed by pain in the back and limbs. The temperature rapidly rises from 2 to 7 degrees; headache and injection of the conjunctiva are present, and nausea, vomiting, and even delirium are common. Dyspnœa and cardiac irregularity are occasionally to be noted. The pulse becomes rapid, hard, and tense,—vibrating. After a time a pronounced perspiration succeeds, and with this the temperature lowers and more or less relief is experienced. The pulse grows less frequent and less tense; the temperature diminishes, but thirst continues unabated. After six to twelve hours the fever subsides, leaving the patient weak; but convalescence, as a rule, is established in a day or two. In some cases the patient has a recurrence of the paroxysm on the following day, or in two or three days, and these may be repeated a number of times. In the absence of definite lesions the attacks soon subside and the patient regains his normal condition.

Differential Features.—From pyelonephritis and suppurative nephritis urinary fever is distinguished by the sudden onset of the latter and the brief duration of the fever; by the history of the case, such as previously healthy kidneys and healthy state of the bladder and lower urinary tract.

From uræmia more difficulty is encountered in making a distinction, since suppression may occur for several days and death result, at least in part, from uræmia. In urinary fever sufficiently severe to cause death, it does so more rapidly than does uræmia. The absence of coma and convulsions, the retention of consciousness, etc., exclude uræmia. Septicæmia is distinguished by its slower onset, low typhoid character, and continuous progressive course without intermission.

HYDRONEPHROSIS.

The above term was first employed by Rayer to denote the overdistension of the kidney with urine. It is, in fact, a result of mechanical obstruction to the outflow of the urine, the obstruction being located in the ureter, bladder, or urethra. This disease should be carefully distinguished from pyonephrosis,—a condition also of distension of the kidney with urine plus purulent matter. It should also be distinguished from large cysts of the kidney the contents of which are fluid, but not urinous.

Hydronephrosis in its pathological significance has been best expressed by Terrier and Baudouin as "*an aseptic dilatation of the pelvis by urine, the flow of which is obstructed by some mechanical obstacle.*" About 35 to 40 per cent. of the cases are congenital, the remainder being acquired. The congenital causes comprise twists of the ureter upon its axis, undue obliquity of the ureteral opening into the bladder, reduplication, valve-like folds of the ureteral mucous membrane, and imperforate ureter. The acquired causes include cancer of the pelvic organs, notably of the ovaries; hydatids and other growths within or impinging upon the ureters; calculus in the ureter; traumatisms, including renal dislocations, twists, etc.; abdominal tumors, vesical growths involving the ureteral openings, and obstructive diseases of the prostate.

The Urine.—The quantity of urine varies according to the degree of obstruction, and whether the disease be confined to one or both kidneys. In the milder forms of obstruction the quantity of urine varies greatly, there being periods of diminution followed by periods of increased flow. On the whole, the volume of urine is diminished. The urine is of low specific gravity, and reduced in its solid constituents,—conditions which, as Dickinson has pointed out, always exist with urine secreted against pressure. The urine sometimes contains blood, which is discharged with great pain (renal colic), especially if clots be present. Slight albuminuria is usually present, though this is not invariably so. The urea is markedly reduced, both relatively and absolutely; the phosphates are greatly reduced in most cases, while the chlorides and sulphates suffer the least diminution. Sedimentation of the urine shows excess of epithelium, in which the spindle-shaped and angular cells predominate. Renal casts, as a rule, are absent, but a few scattering pus-corpuscles and blood-discs are usually present.

Prominent Clinical Features.—Dull, aching pain is usually present in the renal region, with some increased frequency of micturition. Tumor is present in most cases, gradually encroaching on the median line and downward toward the iliac fossa. About one-fourth of the cases of single hydronephrosis extend beyond the median line, and in a considerable number of these tumor occupies a very considerable area of the abdominal cavity. Sudden diminution in size of tumor, coincident with excretion of unusual quantity of non-purulent urine, may be considered diagnostic.

Vomiting sometimes occurs during periods of retention, and sometimes a urinous odor may be observed in the perspiration at such times. Constipation is a frequent result of pressure upon the colon; more rarely diarrhœa may be present from the same cause. So long as the hydronephrosis be single and the remaining kidney be sound, there is absence of uræmic symptoms. If, however, the remaining kidney be diseased or the hydronephrosis be bilateral, suppression of urine and uræmia are liable to result at any time and prove fatal.

Differential Features.—Hydronephrosis is to be distinguished from other abdominal tumors by the presence of urea and uric acid in the fluid withdrawn by aspiration, and by the abrupt diminution in the size of the tumor coincident with copious discharge of urine. Hydronephrosis may be confounded with renal cancer or cystic degeneration of the kidney. In hydronephrosis the tumor is evenly and distinctly fluctuant, no dullness on percussion being observable throughout its extent. The tumor, furthermore, does not conform to the shape of the kidney; it is usually unattended by dropsy, hæmaturia, or cachexia. In cystic disease the tumor is bilateral, non-fluctuant, preserves the form of the kidney, is painless, sometimes attended by dropsy, nearly always associated with hæmaturia, and the tumor does not rapidly change in size.

In cancer the tumor is unilateral, non-fluctuant, irregular in form, rapid in growth, attended by severe pain; copious, recurrent, and persistent hæmaturia occurs, and in late stages pronounced cachexia is present.

PYONEPHROSIS.

Pyonephrosis is a dilatation of the renal pelvis and calices of the kidney with purulent urine, or, in other words, it is hydronephrosis with suppurative inflammation added. In marked cases the suppurative process extends beyond the calices and results in compression, atrophy, and destruction of the parenchyma of the kidney. The causes are the same as those of hydronephrosis plus suppurative inflammation.

The Urine.—Pus is always present if the obstruction be incomplete. If complete at times, and not at others, pus will appear intermittently in the urine if the disease be unilateral. The quantity of urine voided will depend upon the degree of pressure exerted. If the ureter be blocked, as often occurs for some periods of time, the urine will be greatly diminished in volume during the period of obstruction. If only partly occluded, the quantity of urine, as well as that of pus, will vary even during twenty-four hours. If the obstruction be temporarily relieved, large quantities of urine are voided which contains blood and pus, while during the period of occlusion the urine is clear and normal in appearance, unless the disease be bilateral.

In the early stages of this lesion the urine contains blood (sometimes only in microscopical quantity), more or less mucus, and epithelium and pus. The urine is usually acid in reaction, of low specific gravity, and contains albumin, as a rule corresponding with the quantity of blood and pus in the urine. As the disease advances, pyuria becomes more pronounced. The urine is still acid, unless in very advanced cases, when sacculation of the kidney occurs, in which case it may become ammoniacal. In all stages the urine is of lowered specific gravity, the solids more or less decreased, and micturition is somewhat more frequent than normal.

Prominent Clinical Features.—The prominent symptoms of pyonephrosis comprise pyuria with constitutional symptoms, such as rigors, evening temperature, emaciation, anæmia, prostration, and, in advanced cases, hectic. If tumor form, it may be elastic and fluctuant or hard, and extend both forward and downward. Pain is present, varying with the size of the tumor and degree of fluctuation. It often appears in paroxysms of intensity,—*renal colic*. Pressure over the anterior of the tumor greatly increases the pain, or develops it, if not before present. On the other hand, lateral pressure may relieve the pain when present. The bowels are usually disturbed, constipation or diarrhœa being frequent. When the ureter becomes suddenly and completely blocked, sharp constitutional symptoms often follow, such as chill followed by rise of temperature, which may reach 103° to 105° F.; profuse perspirations, rapid pulse, quickened respirations, and sharp pain in the affected side. These symptoms usually continue for some time, and are suddenly relieved by a copious flow of urine, which had previously been greatly reduced in quantity.

ACUTE INTERSTITIAL NEPHRITIS.

This disease has been described under several names, viz., "*suppurative nephritis*," "*acute interstitial nephritis*," "*pyelonephritis*," and "*surgical kidney*." It is, in fact, an acute interstitial nephritis with numerous points of suppuration in the kidney, varying in size from mere dots to large abscesses, which may occupy almost the entire organ. It is seldom observed as a primary disease; by far the greater number of cases are secondary and consequent to urethral stricture, prostatic enlargement, large vesical calculi, atony of the bladder, infectious emboli, or traumatisms. It sometimes complicates typhus, typhoid fever, diphtheria, carbuncles, pyæmia, cholera, and like infectious diseases. Obstructive diseases of the urinary conducting channels, with decomposing urine from retention, are strong predisposing as well as exciting causes. Under such conditions careless instrumentation of the urethra and bladder are exceedingly prone to induce acute interstitial nephritis; hence the misapplied term "*surgical kidney*."

The Urine.—This is always cloudy, of pale, dirty-yellowish color, and of peculiarly foul odor. The specific gravity is reduced,—1016 to 1006,—and the quantity of urine is reduced. The reaction may be acid, neutral, or alkaline. If acid, the disease is likely to be limited to the kidney; but if alkaline, pyelitis and perhaps cystitis also exist. Whatever be the chemical reaction of the urine when voided, upon standing it rapidly undergoes ammoniacal decomposition. The normal constituents of the urine are reduced in quantity, notably the urea. Albumin is always present in the urine, though in variable quantity, the amount always exceeding that due to the contained pus and blood.

The urinary sediment is always abundant, and consists, for the most part, of pus, blood, bacteria, organic *débris*, epithelium, and usually casts. The presence of pus is an essential feature of the disease; it is always present and may be very copious in quantity.

The microscope reveals the presence of micro-organisms in abundance, and sometimes finely-formed casts of bacteria are to be seen. A sudden and marked increase in the quantity of pus in the urine, especially if containing recognizable remnants of glomeruli or urinary tubules, denotes the formation of renal abscess.

Prominent Clinical Features.—The commencement is marked by pronounced rigor or a succession of chills followed by rise of temperature, which in the evening may reach 103° to 105° F., while the morning temperature may be below 100° F. Weakness, drowsiness, flatulence, and sense of abdominal fullness follow. Rapid emaciation, pinched features, and dull, leaden, or sallow appearance succeed. In the evening the skin becomes hot and great thirst is present. Profuse perspiration is common; the tongue may remain comparatively clean, but more often it becomes dry and coated with a brownish-white fur. Nausea is frequent, and vomiting occasionally follows. Renal pain and tenderness are usually absent, but considerable pain is present in the limbs and along the spine. In unfavorable cases the symptoms continue until exhaustion succeeds or renal suppuration becomes established, either of which usually terminates life within a few days.

Chronic Pyelitis.

The more acute forms of pyelitis are included in pyonephrosis and acute interstitial nephritis, just considered. The general causes include the acute infectious diseases, such as typhoid, diphtheria, pyæmia, cholera, puerperal septicæmia, and such diseases as carbuncle.

In addition to these we have chronic pyelitis of a more circumscribed character, which may result from an acute attack, or it may be induced by less active causes, being essentially chronic in nature from the beginning. Chronic pyelitis is rarely a primary disease, but is usually associated with other renal lesions or vesical diseases, especially septic inflammations of the lower urinary tract.

Of the local causes gravel constitutes the most frequent source, which may act either by direct irritation or through obstruction. Tuberculosis is a frequent local cause, notably the form of slowly-developing cheesy nodules which set up inflammatory changes both in the pelvic mucous membrane and neighboring tissues.

The various obstructive diseases of the lower urinary channels are frequent causes of inflammation of the mucous membrane of the renal pelvis. These include urethral stricture, enlarged prostate, large vesical calculi, atony of the bladder, etc. The retained urine in such cases is extremely prone to be contaminated with pyogenic germs introduced from without. These organisms, upon introduction, rapidly multiply and spread, causing changes both in the urine and mucous structures, including that of the renal pelvis. These micro-organisms are, for the most part, micrococci, but rod-like forms or bacilli may also be present, both in the urine and mucosa of the renal pelvis.

Pyelitis should not be confounded with suppurating nephritis. This is a common error, due, perhaps, to the fact that they are often, though by no means always, associated; but uncomplicated pyelitis is unattended by the usual general symptoms of septic absorption which are present in suppurating inflammation of the kidney.

The Urine.—The renal irritation consequent to pyelitis induces polyuria; so that the volume of urine is augmented in this lesion. The color of the urine is pale straw-colored, described as "*whey turbid*," and sometimes tends toward a greenish tint. The specific gravity is reduced and the chemical reaction is usually faintly acid. Pus is present in varying quantity, but always the most prominent feature of the sediment (Fig. 43). The solids are relatively reduced owing to the polyuria, but the absolute solids suffer no material changes in amount. Albuminuria is a constant feature of pyelitis, the quantity of albumin exceeding that depending upon the contained pus. The sediment is flocculent, of considerable volume, of greenish-yellow tint, not so viscid or sticky as in cystitis, and, as already stated, is chiefly composed of pus. The pus-corpuscles often exhibit tooth-like margins, notably so in chronic cases. They often become pressed together in the papillary ducts and form masses of round, oval, or long plugs, which are considered characteristic of pyelitis. Epithelium is present only in small quantities. This lesion cannot be diagnosticated by the presence of spindle-shaped epithelium in the urine alone, as has been frequently asserted. In truth, much of the epithelium lost by the mucosa of the renal pelvis breaks down into pus-cells and granular matter. Blood-corpuscles are rarely present, save when the pyelitis is due to calculus, tuberculosis, growths, or entozoa. If, as is usually the case, the pyelitis be unilateral, the urine sometimes presents one or two anomalous features in reference to its chemical reaction. Thus, the urine may be putrescent and offensive from decomposition, and yet remain acid. Again, it is not uncommon to meet with triple-phosphate crystals in the urine which gives a distinctly acid reaction. These features have been explained by the fact that the urine from the sound kidney overcomes the alkalinity of the urine from the diseased kidney as they mingle together in the bladder, and it is thus voided before it has had sufficient time to become ammoniacal. The triple-phosphate crystals met with in the urine under such circumstances often show evidences of their existence in acid urine in their superficial solution, their sharp angles being rounded. The urine in pyelitis is peculiarly offensive,—not merely ammoniacal, but

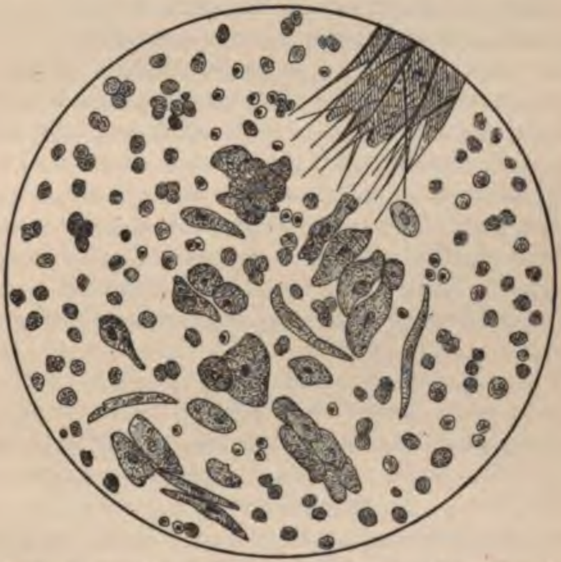

FIG. 43.—URINARY SEDIMENT IN PYELITIS. (After Peyer.)

rather also suggestive of sulphuretted hydrogen,—while in cystitis the odor is almost purely ammoniacal. Once experienced, the odor of the urine in pyelitis may afterward be recognized as characteristic when present. This property of the urine, however, varies from time to time, and may even be temporarily absent if the ureter of the affected side become blocked.

Prominent Clinical Features.—These comprise aching, dragging pains, central in the lumbar region, but often radiating along the course of the ureter toward the bladder. The pain is not usually severe, is always increased by deep pressure by the finger-tips, and it may be absent at limited, but considerable, periods of time, and it is increased by exercise. Renal colic is apt to form a feature of the history of this lesion, but especially so when the cause is connected with stone, hydatids, tuberculosis, or cancer. Micturition is more frequent than normal, but it is rarely attended by pain, being rather of reflex character. Occasionally, when the ureter becomes blocked and retention of urine occurs in the affected organ, elevation of temperature occurs with the usual febrile symptoms. The fever is nocturnal, usually of mild grade, and often accompanied by cutaneous eruptions not unlike rötheln.

MOVABLE KIDNEY.

The subject of misplacements of the kidney embraces three conditions of the organs: 1. *Simple misplacements of the kidney.* 2. *Movable kidney.* 3. *Floating kidney.*

Simple misplacement of the kidney is met with either as a congenital or acquired condition. Of the congenital order, the horseshoe kidney is most common; the next most frequent congenital malposition is above the sacro-iliac synchondrosis. The suprarenal bodies are often found congenitally misplaced, especially when the kidneys are higher than normal. Congenital misplacement is most often unilateral, and most often involves the left kidney. Simple acquired misplacement may be brought about by pressure of adjacent organs, such as enlargement of the spleen or liver, or from pressure of large morbid growths. Tight lacing has been alleged as a frequent cause of downward displacement of the kidney, but this is now considered as an exceptional cause. Both acquired and congenitally misplaced kidney may be mistaken for new growths. As a rule, misplaced kidney, if unattended by mobility, gives rise to no special symptoms, and is only observed at the autopsy. It therefore deserves no extended study by the clinician.

Movable kidney differs from *floating kidney* in that the former lies loosely between the peritoneum in front and the muscular wall of the abdomen behind, while the floating kidney is inclosed in peritoneum, which forms a "*mesonephron.*" The floating kidney, therefore, floats within the abdominal cavity, as do the intestines. Movable kidney, as a rule, is acquired, while floating kidney is always congenital. Movable kidney is most common in females. The right kidney is about twelve times more frequently movable than the left, which is probably due to the weight and unyielding nature of the liver, the greater length of the right renal vessels, and the less firm attachments to the colon on the right, together with the greater right tension and strain in right-handed people. Movable kidney is bilateral about once in every twenty cases. It is most frequent from 30 to 40 years of age, a large proportion of the cases occurring in women who have rapidly borne children.

Absorption of the fatty elements of the renal capsule is now regarded as the most common predisposing cause of movable kidney, and this is borne out by the remarkable frequency of its occurrence in spare subjects. Lastly, movable kidney is often the result of dislocation from falls or blows.

The Urine.—It has been denied by many authors that movable kidney produces any effect on the character of the urine. Those who have seen much of such cases, however, will scarcely have failed to observe frequent urinary disturbances, which form an important, almost essential, part of the pathology of this condition. The urine is often scanty, high colored, and usually deposits more or less sediment; at other times it is more copious than normal. Hæmaturia is not unfrequent in movable kidney. The twists of the ureter attendant upon renal mobility necessarily entail more or less interference with the circulation. The duration and degree of this interference determine the degree of suppression, the discharge of blood, presence of albumin, epithelial denudation, and pyelitis. Suppression of urine usually occurs only at short periods, because the loosening of the renal capsule from the posterior abdominal wall permits the renal pelvis and part of the ureter to also separate from the abdominal wall and follow the renal movements. Thus, the obstacle to the escape of urine is more easily overcome by pressure of retained urine within the renal pelvis.

Diminished excretion (25 to 30 ounces) and short periods of suppression, followed by short periods of copious flow of pale-colored urine of low specific gravity, are common features of this condition, though these are not so marked as in pyonephrosis. During periods of suppression mild uræmic symptoms have been noted; these are rarely pronounced, because the flow is soon restored. The urine very often contains a small amount of albumin, owing to the circulatory disturbances in the kidney.

Prominent Clinical Features.—The chief clinical symptoms of movable kidney are: sensations of dragging weight in the side; occasional sense of movement; severe paroxysms of pain, like renal colic; pain of a dull, aching character; neuralgic pains in trunk-nerves of the affected side. Nausea and vomiting are often present, and may be severe. Intestinal disturbances are common, such as diarrhœa or constipation. Loss of appetite, weakness, debility, flatulence, emaciation, and depression are frequent features observable. Nearly all the symptoms are increased by movement or standing, while they are relieved by rest and quietude. Menstruation and pregnancy usually aggravate the symptoms. Manipulation of tumor causes peculiar sinking or fainting sensations, often attended by nausea. The tumor possesses more or less mobility.

Differential Features.—Limited contractions of the recti, transversalis, or abdominal oblique muscles sometimes give impressions of smooth, oval tumors, which may even disappear on pressure, not unlike movable kidney. Anæsthesia and strong percussion over tumor will usually distinguish the true condition.

A tumor of the liver, or distended gall-bladder, or a liver deformed from tight lacing, or an hypertrophied liver may give rise to similar percussion-sounds, as well as similar gastric disorders, and vague abdominal sensations and pain not unlike movable right kidney. Distinction is most difficult, but may be accomplished by palpation, urinary changes or their absence, etiological elements, and by results of treatment. Percussion cannot be depended on in these cases alone; if the tumor can be completely separated from the liver by palpation, it goes far toward establishing movable right kidney.

Movable spleen is distinguished from movable kidney by the former lying immediately beneath the abdominal wall throughout all movements, while a kidney when pushed upward retreats from the abdominal wall beneath the intestines. The percussion-note over the spleen is, therefore, always dull, while over the kidney it is dull tympanitic or tympanitic.

The distinction between uterine or ovarian tumor and movable kidney is determined chiefly by the *direction* of mobility. If mobility can be made to extend to lumbar region without pain, tumor of the uterus or ovaries may be excluded. On the other hand, movable kidney must not be excluded by mobility toward the pelvis, as such tumor may exceptionally be renal. If the renal artery can be grasped and pulsations felt, the diagnosis becomes clear. Capability of replacement of kidney with disappearance of tumor renders renal source of tumor certain.

CYSTITIS.

Much confusion has existed as to the nature of cystitis in consequence of the diversified classifications of this affection. Writers speak of *purulent cystitis*, *hæmorrhagic cystitis*, *cystitis of the neck*, *cystitis of the body of the bladder*, and *catarrhal cystitis* of several grades. *Acute cystitis* and *chronic cystitis* are employed as denoting intensity or duration of inflammatory process, rather than the character of the lesions present, and as such the terms are convenient for descriptive purposes.

In the light of modern investigations and present pathological knowledge cystitis is coming to be better understood and its signification has assumed more accurate and definite meaning. In all its varying phases cystitis must now be considered as a local bladder infection by bacterial germs. Normal urine, as already pointed out, is an aseptic fluid characterized by the absence of septic germs, while cystitis is always associated with the presence of septic micro-organisms in greater or less abundance.

The same causes which bring about local infection elsewhere may be looked for to explain the presence of bladder infection. Comprehensively considered, they include the following conditions: Weakened vitality of the tissues; favorable soil for development and the presence of micro-organisms possessing pyogenic powers. If we consider for a moment the many conditions to which the urinary bladder is exposed, which tend to weaken its resisting power to the action of germs; the many sources of exposure to local infection, and the favorable medium the urine constitutes as a culture medium for many pyogenic germs, it no longer seems strange that cystitis is one of the most frequent diseases of the urinary tract. Since the discovery of the micrococcus ureæ by Pasteur, thirty-five years ago, to the present time, a large number of micro-organisms have been discovered in pathological urine. Although many of these possess no pathogenic powers, a number of them are, without doubt, closely associated with cystitis in the relationship of cause and effect.

The older theory, that cystitis is set up by ammonium evolved in the decomposition of the urine by the micrococcus ureæ, is no longer accepted. It has been conclusively demonstrated by Guiard and Guyon that ammoniacal fermentation of the urine in the bladder takes place as a *result* of cystitis, and in the absence of the latter the former does not occur. The question, then, of the local etiology of cystitis must be narrowed down to local infection of the bladder by pathogenic germs, and the results of their action constitute cystitis.

Of the many etiological factors which favor bladder-infection may be mentioned the following: Retention of urine, trauma, deep gonorrhœa, stricture of the urethra, prostatitis, calculus, morbid growths, exposure to cold, sexual excesses, gout, paraplegia, etc.

The Urine.—Pus is present in the urine as the most essential feature of cystitis, its absence being proof that the bladder is uninflamed. The quantity of pus present depends upon the degree and extent of the cystitis and the length of time cystitis has been established. Early in the lesion the quantity is small, sometimes observable only under the microscope. If the urine be acid the cystitis is recent, and the pus readily settles. If the urine be alkaline—ammoniacal—the pus settles in a viscid, sticky mass, the cystitis is chronic, often termed "*chronic catarrhal cystitis.*" Blood is nearly always present in acute cystitis, and sometimes also in the chronic lesion. It is increased in quantity by movements or standing. In acute cases it is due to congestion; the quantity is comparatively small, and for the most part it appears at the close of micturition. In tumors and varicose conditions of the vessels, blood is mixed more uniformly with the urine, and the quantity may in such cases be large.

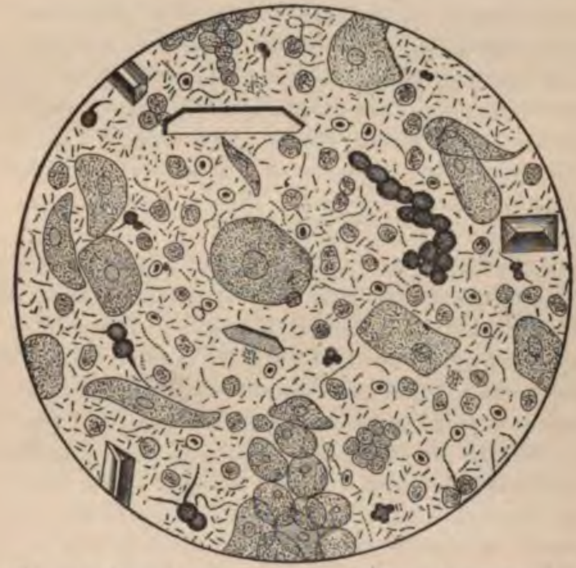

FIG. 44.—URINARY SEDIMENT IN CYSTITIS. (After Peyer.)

The quantity of albumin in the urine is inconstant in this lesion. In the early course of the disease it is usually due to pus or blood, and consequently the amount is small. In chronic cases the quantity is more considerable, since denudation of the vesical mucous surface permits of more ready escape of blood-serum. The reaction of the urine is usually acid in the early course of the disease as well as in mild cases; while chronic, long-continued cases are mostly characterized by alkaline urine from volatile alkali. Accompanying the ammoniacal changes, more or less copious deposits of triple-phosphate crystals are to be found in the urine. In addition to this, amorphous phosphates are often present in considerable quantity, and less frequently, also, are urates.

Recent cystitis differs from the chronic form as follows: In the former the quantity of urine is usually normal; color is dark; the reaction is acid *when voided*, quickly becoming alkaline after it is voided; the specific gravity of the urine is usually normal; the appearance is turbid and smoky. Microscopical inspection shows the presence of vesical epithelium, pus, often blood, and bacteria; and on standing a few crystals of triple phosphates usually are observed.

In chronic cases the quantity of urine is about normal; the color is light, the reaction alkaline, the specific gravity somewhat lowered, and albumin is usually present. Microscopical inspection shows the presence of pus usually in abundance, sometimes blood, bacteria always, and vesical epithelium. The appearance of the urine is turbid, the odor is ammoniacal, and the sediment sticks to the glass or vessel upon standing. The micro-organisms most often met with in cystitis are as follow: The *staphylococcus pyogenes aureus*, *albus*, and *citreus;* the *streptococcus pyogenes;* the *urobacillus liquifaciens septicus;* and the *bacillus coli communis*. These are all pathogenic germs. Those most frequently met with are the *bacillus coli communis*, and next is the *staphylococcus pyogenes aureus*.

Prominent Clinical Features.—Frequent micturition, pain, and pyuria are the most constant symptoms of cystitis. Frequent micturition varies with the intensity of the disease and the sensitiveness of the bladder. In acute cystitis the desire to micturate is nearly continuous. The frequency is increased upon standing or walking, while rest tends to relieve it. The pain also varies according to the acuteness of the attack. The pain is often very intense at or just before the beginning of micturition, is more or less relieved during the flow of urine, while at the close of micturition, and immediately following, for a few seconds the pain becomes greatly increased. The latter is most notably the case when cystitis is associated with stone or prostatitis. In cases of highly ammoniacal urine considerable pain is often experienced during the act of micturition. There is more or less discomfort, sometimes amounting to pain, with sensation of weight above the pubis, in cystitis, irrespective of the act of micturition. The bladder is sensitive to rectal touch, as well as to instrumentation, and also to distension by injections of fluids, however bland they may be. Hæmorrhage, if present, indicates, as a rule, the more acute grades of cystitis, unless in large amounts, which are more common in chronic forms. Constitutional symptoms are absent unless the disease be associated with tuberculosis, malignant disease, etc.

VESICAL STONE.

The etiology and symptomatology of calculous disease have already been considered in detail. More than one-half the cases of vesical stone met with in hospital practice occur before the age of puberty; about 22 per cent. occur between the ages of 50 and 70 years; while not above 2 per cent. are met with above 70 years of age. The statistics of Sir Henry Thompson, as well as those gathered from large hospitals, substantially confirm the above proportions. In private practice, however, the above proportions are almost directly reversed. Thus, in Sir Henry Thompson's private practice the patients between 50 and 70 years of age comprised 65 per cent. of the whole; and those over 70 comprised 22 per cent. of the whole; while those under 16 comprised less than 1 per cent. From these facts Sir Henry Thompson draws the following deductions: "Insufficient food, clothing, and fresh air, the necessary accompaniments of poverty, appear to encourage calculous formations among children, but not among adults. Habits of self-indulgence, in relation chiefly to diet and indolence, encourage calculous formations in early adult males, but the children of such parents are not affected. Hard physical labor and a regimen which necessarily contains simple diet, largely cereal, with animal food in small proportion, even although often associated with intemperate habits and unhealthy dwellings, discourage calculous formations among all classes of the community alike." The foregoing only applies to primary formations.

The Urine.—Before the onset of cystitis the urine may remain but little changed from the normal. The quantity is normal; the specific gravity is not materially altered; the urine remains clear, tending to increased color, perhaps, and the reaction may be either acid or alkaline. The history often reveals habitual deposits of red sand or white, gritty powder for months or years before special symptoms appear. In the early stages, when, to all appearances, the urine remains normal, the microscope usually reveals the presence of uric-acid crystals or those of calcium oxalate, together with scattering blood- and pus- corpuscles. Cystitis sooner or later appears, when the urine becomes cloudy from increased pus formation, together with the presence of epithelium, crystals of uric acid, calcium oxalate, triple phosphates, or amorphous urates or phosphates. If the urine remain acid the crystalline deposit will be uric acid or calcium oxalate, often both together. If the urine be alkaline the crystalline deposit will consist of triple phosphates, and the pus deposit will be more or less viscid and sticky. The degree of pyuria indicates the extent of denudation or ulceration of the mucous surface of the bladder. Blood is often present in variable amount, but rarely excessive. Albumin is always present in the urine if cystitis co-exist, and frequently in excess of the contained pus or blood. Micro-organisms are present also in all cases attended by cystitis, and for the most part of the same order.

Clinical Features.—Pain is present as one of the most typical features, tending to reflection along the urethra, in the testes, or down the thighs. Pain is sharply increased at the close of micturition and for a few seconds afterward, especially noticed in the glans penis. Spasm of the bladder is common at the close of micturition. The pain is always increased by the erect posture and by motion, including riding, walking, and even by turning in bed sometimes. There is more or less increased frequency of micturition, augmented by motion and relieved by continued rest and recumbency. Micturition is sometimes suddenly shut off in the middle of the act, in consequence of the stone rolling forward over the urethral inlet. On lying upon the back this symptom is relieved.

Hæmaturia is the rule in this disease, the blood usually being clear, bright in color, and usually consists of a few drops at the close of micturition, the urine at the beginning of micturition being mostly free from blood. Sometimes hæmorrhage is more considerable, and the blood becomes more generally diffused through the urine in such cases. Hæmaturia is increased by movement, as walking and riding, etc., and is relieved by rest and recumbency, and therefore it is always less in the morning and more in the latter part of the day or in the evening. To complete the diagnosis exploration is often necessary. This may be done (*a*) *per vaginam* or *rectum* by means of the finger; (*b*) by means of the vesical sound; (*c*) by means of the cystoscope; (*d*) by digital examination through the dilated urethra in women. The most satisfactory methods are those of the sound and the cystoscope.

VESICAL TUBERCULOSIS.

Primary tuberculosis of the bladder is comparatively rare, and when present it invariably begins in the trigone. More often it results from extension of tubercular disease from the prostate, testes, or recto-vesical fold of the peritoneum, less often by infection from the upper portions of the urinary tract. The bladder may become infected from above either by direct extension of the disease along the ureter or by inoculation through the urine from tuberculous kidney.

When infection occurs from surface inoculations through the urine from above the symptoms rapidly supervene and the disease is acutely progressive. On the other hand, when the disease is primary the symptoms are more slow in development and the course of the disease is more apt to be protracted.

The Urine.—Blood is usually present in the urine in this lesion in small amount, often transitory and recurrent, a few drops often following the close of micturition, as in stone. Sometimes, however, hæmaturia is pronounced, in consequence of ulceration about the tubercular deposits. The urine contains small quantities of pus from the beginning, which gradually increase until appreciable deposits thereof are regularly present.

The urine is murky, of light color, of normal specific gravity, and it is usually feebly acid or neutral until it becomes ammoniacal from the presence of cystitis. The urine is not especially offensive, although it may be ammoniacal, as just stated.

With the occurrence of cystitis all the features of the urine characteristic of that disease supervene, and that in the most pronounced form. These include pyuria, hæmaturia, deposits of triple-phosphate crystals, amorphous phosphates, epithelium in states of progressive necrosis, and micro-organisms in abundance.

Prominent Clinical Features.—These patients are young, usually from 15 to 30 years of age, with family histories of tuberculous disease in some form. The early symptoms consist of increasing frequency of micturition for a few months, especially during the day. Blood appears in the urine, and with this the patient begins to rise at night to micturate. The pain in micturition is referred chiefly to the mid-penis. Sharp, vesical tenesmus becomes developed as the disease proceeds, and in such cases the pain is increased at the finish of micturition. The constitutional symptoms include debility, emaciation, weakness, elevation of temperature in the evening, and night-sweats. With these symptoms are often associated tuberculosis of the lungs, joints, glands, or elsewhere.

Differential Features.—Tubercular cystitis in many of its manifestations resembles stone in the bladder. Tuberculosis of the bladder, however, is more frequent in youth; the family history is often tuberculous; the irritability of the bladder is often marked at night, greatly disturbing the patient's rest; hæmaturia is often sudden and without apparent cause, being less dependent upon exercise; there is greater relief from pain at the close of micturition; pain is in mid-penis, rather than in glans penis; there is persistent post-scrotal perineal pain; the urine is light in color, murky, inodorous, and purulent from the beginning, and periods of quiescence if the symptoms do not correspond to quiescence and rest. In late stages evening temperature is present, marked constitutional symptoms arise, implication of epididymis is common, and knobby or shotty feel of prostate *per rectum* points to the tubercular character of the disease.

CANCER OF THE BLADDER.

The great majority of malignant growths of the bladder are of the carcinomatous order. Carcinoma of the bladder usually begins at the base of the organ, or, more accurately speaking, at the lower third of the organ. It manifests a peculiar tendency to long remain a local disease, with little tendency of extension to neighboring structures. This has been explained by the scarcity—according to some, the absence—of lymphatics in the bladder-walls.

The Urine.—The urine contains blood in the vast majority of these cases. Seldom being entirely absent from the urine, it is subject to periods of marked augmentation without any apparent exciting cause. Attacks of marked hæmaturia are quite as likely, therefore, to occur at night as during the hours of exercise through the day. The quantity of blood is often greater than in almost any other disease of the urinary organs; so that the bladder is liable to become partly filled with large blood-clots. As a rule, the quantity of blood in the urine irregularly, but continuedly, increases as the disease advances. The color of the blood is usually bright red, especially when it is abundant, but if in small quantity it may be dull red or brownish in appearance. The blood is not intimately mingled with the urine as it is in renal hæmaturia.

The urine often contains shreds or detached bits of the morbid growth, which may even be noticeable to the patient. To the naked eye these appear as "washed-out" bits of tissue, which in reality they are, and they vary in size from minute specks to pieces as large as a pea or small bean. Their presence merely indicates the presence of some growth without indicating its character. No trustworthy inferences are to be drawn as to the nature of these shreds from microscopical examination, since both malignant and benign growths of the bladder may present papillary surfaces of practically the same microscopical appearance. Since, however, such shreds are most frequently the product of papillomata or malignant growths, their presence may be considered as simply presumptive of one or the other of these forms of growth.

The urine nearly always contains an abundant sediment in malignant disease of the bladder, of which epithelium constitutes a prominent feature. The epithelium is of small or moderate size, but with very large and plainly-visible nuclei. The quantity of urine remains normal, as does the specific gravity, save in late stages, when the latter becomes somewhat reduced. The urine is turbid, often brownish red, and the reaction is acid until cystitis becomes established; with the appearance of the latter there is pyuria, ammonuria, bacteriuria, and the usual accompanying symptoms.

Prominent Clinical Features.—Pain is a prominent and early symptom, usually preceding the hæmaturia. The character of the pain is often sharp, radiating to the thighs, above the symphysis pubis, or in the post-scrotal region. The pain is not especially increased by movements. Fenwick has recently called especial attention to the fact, as he claims that, if the disease do not invade the trigone, pain may be practically absent until a late period of the disease. This may account for the occasional absence of pain almost throughout the disease. Frequency of micturition is more or less pronounced from the beginning, and this is attended by pain, which is most notable just before the beginning of the flow. Rectal examination develops local tenderness and patches of induration.

BENIGN VESICAL GROWTHS.

The chief varieties of benign growths met with in the bladder are *papilloma*, *myxoma*, and *myoma* Of these, *papillomata* are by far the most frequent. These consist of proliferations of the natural structure of the vesical mucosa, forming papillæ or protrusions covered with cylindrical epithelium. Sometimes these papillæ are long and slender and float in the urine in numerous filaments from a common base or stalk. Examined in a dry state they collapse and form a soft, "*strawberry-like*" mass. The base or pedicle always contains more or less fibrous tissue, and usually some non-striped muscular fibres. Sometimes the growth expands to form a polypoid-like mass of more decided firmness, or it may have a wider attachment to the bladder. Again, it sometimes appears expanded into several bunches not unlike cauliflower. When the fibrous elements are numerous the structure is more dense, and this form has been termed "*fibrous papilloma.*" The latter are, for the most part, tumors of some considerable solidity, and often have comparatively limited papillary margins.

The *myxoma*, or simple mucous polyp, is rarely met with in the bladder; thus far, only in childhood. Sometimes it is congenital. The growth is that of fibroid undergoing mucoid transformation. This growth is single, pedunculated in form, and resembles the ordinary naasl polypus.

Myoma is only occasionally met with in the bladder. It is usually of moderate size, with wide base, round or oval in form, rather firm in consistence, and chiefly made up of muscular fibre, evidently the outgrowth of the muscular coat of the bladder. The last two described growths are so uncommon in the bladder that for practical purposes papillomata only require special consideration.

The Urine.—The most important feature of the urine in papilloma of the bladder is the presence of blood,—hæmaturia. This occurs early, and at first in paroxysms, followed by more or less lengthy intervals of absence. Commencing insidiously, often appearing in the form of small dark clots, "*like flies*," appearing and disappearing alternately for a few days at each time; or again, the urine, instead, may appear slightly blood-stained, or a little clear blood may appear at the close of an otherwise micturition of clear urine; or, again, the whole urine voided may appear bloody,—dark "*coffee-colored.*" The hæmaturia usually presents these various types in succession, without other prominent features, for long periods of time,—often for years. Sooner or later, however, attacks of more or less profuse hæmorrhage occur and recur as the growth increases. The blood is not of pronounced arterial color, but more inclined to darker shades. Aside from the presence of blood in the urine, the latter is not otherwise especially altered in its physical characters; the specific gravity and volume remain about normal; the solids are relatively and absolutely unchanged; and the urine remains acid, though often feebly so, until late stages, attended by cystitis, when the reaction may become alkaline.

The urine contains considerable sediment of a finely-flocculent nature, brownish red in color for the most part, and contains blood-corpuscles, more or less pus, epithelium, and often ragged shreds of tissue. The deposit of epithelium from the vesical mucosa is a prominent feature of the sediment, often exceeding that in any other condition. With regard to the shreds often voided with the urine in these cases, it was formerly held that microscopical examination of these readily established the nature of the growth. Unfortunately, however, more extended experience has shown that, while the epithelial character of these pieces is easily enough recognized, yet, in consequence of the fact that any bladder-growth, benign or malignant, may possess a peripheral epithelial fringe, no positive deductions can be drawn from their recognition. We are only able to say, presumptively from these, that papilloma is most probable, because it is most frequently attended by the appearance in the urine of those structures recognized as epithelial formations.

Prominent Clinical Features.—The most prominent symptoms are long duration of hæmaturia without marked pain or other associated symptoms. In other words, hæmaturia precedes, for longer or shorter periods, vesical symptoms, such as pain and frequent micturition Some slight increased frequency of micturition develops after a time, with tendency to increase with the progress of the disease. Pain is scarcely ever a pronounced feature of the disease, usually only so when obstruction occurs from clot or growth situated near the margin of the urethra, when it may stop the flow of urine. In cases of this order tenesmus, frequent micturition, and pain become prominent, and may even precede the hæmaturia. The general condition of the patient remains normal, save, perhaps, anæmia, which is apt to result to a greater or less extent, according to the amount of the hæmaturia.

SECTION XI.

THE URINE IN OTHER DISEASES.

SIMPLE PYREXIA.

CERTAIN changes in the character of the urine in pyrexia are sufficiently constant to merit the term "*pyrexial urine*" often employed. Generally speaking, these comprise diminution in quantity or, more accurately speaking, deficiency of water; increased color, due to increase of pigment, both relative and absolute; increased acidity, and high specific gravity. In addition to these physical changes in the urine, provided no accidental circumstances interfere, more important changes take place in the composition of the urine. Among the most prominent of these changes is a decided increase, both relatively and absolutely, of the nitrogenous elements, viz., urea and uric acid. Since, for the most part, but little food is taken in pyrexial states, and the urea and uric acid rise considerably above the healthy range, we must conclude that the pyrexial state entails a more or less pronounced waste of tissue. While the amount of uric acid excreted varies in different forms of pyrexia as well as in different cases of the same fever, it is undoubtedly more uniformly increased than is any other urinary constituent. This increase of uric acid is proportionately independent of urea, which seems somewhat paradoxical considering that they are both derived from the same tissue-base. In addition to the increase of uric acid and urea, hippuric acid is often present in the urine in large quantity as a consequence of the pyrexial state, indicating, in all probability, a disturbed function of the liver.

The increased excretion of pigment is chiefly due to the destructive metamorphosis of the red blood-corpuscles, the latter being a well-known result of nearly all forms of fever. As might be expected, considering the excess of uric acid and urea, the sulphates are also markedly increased in pyrexia, constituting another evidence of the destructive metamorphosis of nitrogenous (sulphur-holding) tissues.

The chlorides and phosphates, as a rule, are reduced, both relatively and absolutely, in pyrexia. With regard to the former the diminution is probably due, at least in part, to retention; but as regards the phosphates (save in cases of acute inflammations of the nervous or muscular tissues) there is undoubtedly deficient excretion.

As a whole, then, pyrexia entails an excessive excretion of solids by the urine. This excessive excretion begins with the onset of fever, and usually maintains a parallel ratio with the temperature; in short, the presence of the latter invariably implies the former. The urine often contains a small percentage of albumin in simple pyrexial conditions, and the same may be said of acetone.

The urinary sediment in pyrexia is often considerable in amount, and consists of uric-acid crystals, urates, sometimes scattering hyaline casts, a few leucocytes, and epithelium. Aside from the modifications of the above features of the urine by special forms of fever, typical pyrexial urine is subject to certain variations through certain special circumstances, as follow: When, during the course of a fever, an organ becomes the seat of disease, where tissue-changes furnish special urinary products, the products may appear in the urine in excess. As examples, note the increase of phosphates in the urine in inflammatory diseases of the nervous system, and the increase of bile-acids in hepatitis. The overaction of other eliminating organs may disturb the type of febrile urine. Thus, the diarrhœa of typhoid fever modifies the character of the urine, as likewise does the sweating stage of intermittent fever. These are a few of the influences that may produce special variations of the febrile type of urine to a limited degree; but, on the whole, the general pyrexial characters stand out with sufficient prominence for general recognition.

It may be stated, as a general rule, that the amount of tissue-metamorphosis, as indicated by the excretory waste in the urine in fevers, constitutes a good indication of the severity of the disease,—often, indeed, better than the thermometer or pulse.

Upon subsidence of pyrexia the urine assumes directly the opposite characters of the pyrexial state. The chlorides become increased, while the urea, uric acid, phosphates, and pigments are below the normal range. The volume of urine is increased. In short, everything points to delayed metamorphosis, conservation of tissue, and repair.

ACUTE INFECTIOUS DISEASES.

Typhoid Fever.—The quantity of urine is diminished about 50 per cent. during the febrile stage of typhoid, and the volume gradually rises to normal in the third, fourth, or fifth week. The specific gravity of the urine ranges from 1025 to 1030, occasionally reaching as high as 1040. The quantity of urea is increased 25 per cent. or over; as high a range as 78 grammes per day has been recorded. In cases of marked splenic enlargement, copious hæmorrhages, and complicating nephritis the quantity of urea becomes lessened instead of increased. The chlorides suffer marked reduction, especially during the first week, but they gradually increase as convalescence approaches, while with urea this order is reversed. The uric acid is uniformly increased, the increase being relatively greater than that of urea. The gross amount of uric acid increases usually until about the end of the second week, when it reaches about double the normal range. Deposits of urates are common. The phosphates are somewhat diminished, and the pigments are increased relatively and absolutely. The reaction of the urine is sharply acid when voided, but often rapidly turns alkaline upon standing, owing to ammoniacal transformation of the large output of urea.

Albumin is present in the urine in a large proportion of the cases of typhoid fever, probably in the majority. Few observers place the proportion less than 20 per cent. of the whole, while some claim to have found it in nearly all cases. The author's observations lead him to conclude that albuminuria is present in from 70 to 80 per cent. of all cases of typhoid. The quantity of albumin in the urine is usually small; but occasionally it is decided in quantity, and is attended by nephritis. In such cases the prognosis of the disease is always to be considered grave. In most cases the albuminuria is temporary, setting in soon after pyrexia becomes established and subsiding soon after the latter disappears. In a very considerable proportion of the cases, however,—larger than has been generally supposed,—albuminuria fails to subside with pyrexia, and becomes permanent. Leucin and tyrosin are usually to be found in the urine in typhoid, although in no very decided quantities.

Renal casts, epithelium, and blood are frequently seen in the urine. Indeed, with regard to casts, it is probable that they are nearly always to be found during the first and second weeks, if carefully sought. Peptone is often present in the urine of typhoid, especially in the more severe types of the disease.

Thanks to Ehrlich, the diagnosis of typhoid fever is now rendered almost as certain by the urine as is pulmonary tuberculosis by the sputum. The *diazo reaction* of Ehrlich met with many unbelievers at first, as to its reliability as a diagnostic feature of this disease, but overwhelming clinical evidence is now available to prove its undoubtedly great diagnostic value. The following original claims of Ehrlich in reference to this reaction in the urine may be said to have been amply confirmed. "The reaction is found in typhoid fever after the fourth or fifth day, and if absent the diagnosis is doubtful. If the reaction be slight, and only found for a short time, the case will usually be very mild. In simple febrile intestinal catarrh, chlorosis, hydræmia, diabetes, and in diseases of the brain, spinal cord, liver, and kidneys, the reaction is never obtained. The reaction is obtained occasionally in phthisis pulmonalis, rarely in measles, pyæmia, scarlet fever, and erysipelas."

"The diazo reaction in typhoid has no dependence upon the height of temperature, nor is it influenced by the medication. The morning and evening urine give the same intensity of reaction. If the reaction cease in the second or third week, the rule is that the fever will early decline and the further course of the disease be mild. On the other hand, long-continued reaction indicates severity and long continuance of the disease. If relapse occur, the reaction returns if it has previously disappeared."

The importance of the subject justifies a repetition of the essentials of the test, especially since it is strongly probable that much of the diversity of views as to the value of the reaction in typhoid fever has arisen in consequence of faulty methods in performing the test.

The principle of the test depends upon the fact that diazosulphobenzol unites with certain aromatic substances met with in the urine in typhoid, which form analines. The diazosulphobenzol being unstable, Ehrlich obtains it fresh for testing by keeping sulpho-anilic acid in solution with hydrochloric acid. To this solution sodium nitrate is added, which liberates HNO_2 and forms diazosulphobenzol. A full description of the test and the proper method of its manipulation are described on pages 134 and 135.

Scarlatina.—The urine in scarlatina assumes the usual febrile characters, more or less marked in proportion to the degree of pyrexia present. During the first week the volume is reduced, the urea and uric acid are increased, and sediments of urates are precipitated. The chlorides are often decidedly reduced. From the sixth to the eighth day, if the disease proceed favorably, the urine becomes abundant, pale in color, and the general characters approach the normal standard.

But the urine in scarlatina should always be the subject of special observation, in consequence of the fact that it is often especially affected in this disease. This is due to the frequent—almost invariable—implication of the kidneys some time during the course of the disease. Recent observations on an extensive scale indicate that nephritis exists in scarlatina, either in acute form or in mild, evanescent attacks, almost as constantly as the rash or the angina. The number of acute cases of nephritis attended by dropsy and high grades of albuminuria in scarlatina is estimated as about one in every six cases met with,[1] though the proportion varies greatly in each special epidemic of the disease.

As a rule, albumin appears in the urine about the fifth to the eighth day, usually subsiding within about nine days if the disease proceed favorably. The quantity of albumin in the urine is subject to the widest variation, sometimes amounting to mere traces, while, again, the urine becomes almost solid with albuminous coagulum when boiled or treated with albumin precipitants. A few cases are on record in which both nephritis and dropsy were present in scarlatina, while albumin was absent from the urine.

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[1] See section on "Scarlatinal Nephritis" in Bright's Disease and Allied Kidney Affections, by the author. Lea Bros. & Co., Philadelphia, 1886.

Casts are almost invariably to be found in the urine if carefully sought for. In cases proceeding favorably the casts are chiefly hyaline, often preceded by the so-called cylindroids of Thomas. If nephritis become established, the sediment contains the usual elements characteristic of that lesion, more or less pronounced in proportion to its grade. Thus, we may meet with epithelial and bloody casts, as well as granular, in chronic cases. In addition to these, free blood-corpuscles and often large showers of round epithelium are observable. As occasional features, the urine in scarlatina has been found to contain sugar in small amount, hæmoglobin in severe—usually malignant—cases, and sometimes peptone or, more accurately speaking, deutero-proteose, which is usually taken for peptone.

Albuminuria sometimes subsides during the early course of scarlatina, to re-appear later with nephritis. If acute nephritis of pronounced type occur in scarlatina, it usually appears about the eighteenth to the twenty-fourth day; more rarely it arises in the latter part of the second week; more rarely still during the fifth week.

Cholera.—During the algid stage of cholera the urine is more or less completely suppressed. This is due, in the main, to collapse,—weakened circulation,—perhaps to some extent, also, to thickened blood and exudation into the renal tubules. After the cold stage is passed the volume of the urine slowly increases, or it may remain suppressed; in the latter case the patient dies comatose. If the secretion of urine become re-established, it usually does so during the third day from the attack,—forty-eighth to the seventy-second hour. The quantity of the first urine is small, gradually increasing if the patient recover; and on the fifth or sixth day the volume reaches the normal range, or often considerably above. The specific gravity of the urine at first, upon re-appearing, is below normal,—often 1006 or 1008. It may fall still lower at first, but gradually rises to normal as convalescence is established.

The quantity of urea in the urine is greatly reduced in cholera,—in fact, during the first day it may amount to but 2 or 3 grammes, and Bigbie even found it absent. It usually increases somewhat on the second day, and in favorable cases it increases on the third to the sixth day to considerably above the normal range. The prognosis may be considered favorable in proportion to the amount of urea excreted in cases which have passed the algid stage. Uric acid is usually present, though in reduced quantity. It often falls out of solution in a colorless state, owing to the absence of pigment in the urine. The phosphates are greatly reduced in the first urine passed; but, like urea, they become markedly increased with the re-establishment of the urine, and for several days even considerably exceed the normal amount. The chlorides at first are absent, or nearly so; after the fourth or fifth day they gradually return, and increase to, but rarely very much above, normal. The increase of chlorides is considered as even more favorable a prognostic sign than that of urea. As the urine becomes re-established its acidity becomes greatly increased. The normal urinary pigments are nearly absent for the first two days, gradually returning by the sixth day or so to the normal range. The first urine voided in all cases contains so-called indican—indoxyl-potassium sulphate—in marked quantities. Indeed, before the isolation of the cholera bacillus the presence of this substance in the urine was by many considered the best diagnostic indication of cholera where the symptoms were so mild as to cause doubts as to the nature of the disease. Our knowledge of so-called indicanuria, however, has so far increased that we know it is not uncommon in intestinal catarrhs of various kinds, as well as in certain general diseases attended by pronounced albuminous transformation.

The first urine passed in cholera almost invariably contains albumin. So constant is this the case that if the urine were always free from albumin in other forms of diarrhœa, cholera might almost be diagnosticated by the accompanying albuminuria. As a rule, the albuminuria of cholera is of comparatively brief duration, subsiding within a week after its appearance. There is no doubt, however, that the albuminuria sometimes pursues an acute course, accompanied by nephritis, which latter is the direct cause of death by uræmic coma. As a general rule, the quantity of albumin in the urine is proportional to the degree and duration of the algid stage.

Renal casts are invariably to be found in the urine of cholera patients, as well as large deposits of epithelium. With these, blood-corpuscles and uric-acid crystals are usually found. Later on, calcium-oxalate crystals are deposited, either alone or associated with amorphous urates.

Diphtheria.—The urine in diphtheria is decidedly reduced in volume, of high specific gravity, of sharply-acid reaction, and it deposits a copious sediment of uric acid, amorphous urates, oxalates, and sometimes phosphates. The urine contains albumin in over 50 per cent. of the cases of diphtheria, varying in quantity from mere traces to the most pronounced types of albuminuria. The albumin usually appears early in this disease. If of mild grade it sometimes subsides temporarily, and may occur even repeatedly. There is no doubt that the kidneys become implicated in many of these cases, but the tendency to spontaneous recovery from nephritis seems greater than in scarlatina or pneumonia. The quantity of urea is largely increased, and this continues throughout, unless the function of the kidneys becomes much crippled in consequence of associated nephritis. At the height of the disease the quantity of urea is often double the normal range. Renal casts are frequently present in the urinary sediment; less often, blood. Pus sometimes appears in considerable quantity as a consequence of pyelitis, which is often evoked by this disease.

Variola.—In small-pox the urine assumes the usual typical features common to pyrexia, which continue until about the twelfth day. The urea is moderately increased, and reaches its highest average with the highest temperature. Even in the absence of marked temperature and upon a spare diet the urea is still above the normal range. The uric acid is excreted pretty uniformly in excess throughout the course of the disease, and deposits of urates are constant. The chlorides are somewhat, though not decidedly, reduced. The sulphates suffer slight reduction, though to no marked degree, probably only consequent to the lessened quantity of food ingested. The pigment is very considerably increased.

Albumin appears in the urine in about 30 per cent. of the cases of small-pox. It usually appears at the height of pyrexia, though in severe cases it often appears at the onset of the disease. As a rule, albuminuria is only temporary in variola, the tendency to leave behind serious nephritis being comparatively slight, although such results sometimes occur. The presence of bile-pigment in the urine is a frequent and noteworthy fact first observed by Schonlein in these cases. In malignant forms of the disease the urine contains hæmoglobin. In less severe cases hæmaturia is not uncommon, and often of pronounced degree. Casts, epithelium, and other evidences of nephritis are to be found in the urinary sediment in cases associated with albuminuria.

Yellow Fever.—The quantity of urine is markedly diminished from the onset of this disease. In many cases it becomes nearly or even quite suppressed, and in such cases all the manifestations of uræmia follow. The reaction of the urine is usually acid throughout the first stage, and becomes alkaline during convalescence. The color of the urine varies: it may be bright yellow, dirty orange-colored, greenish brown, olive black, or sometimes red from the presence of blood. The urine becomes albuminous almost without exception, and very often highly so. A very close relationship undoubtedly exists between the more serious symptoms of the disease and the associated renal lesions, for in such cases albuminuria is *always* present in the urine, together with tube-casts, epithelium, blood, and the morphological elements common to acute nephritis. In addition to this, all the usual phenomena of uræmia follow in most of such cases, but especially coma. The urea is greatly diminished; sometimes it is totally absent. The uric acid is also greatly diminished, and is even said to be absent in some cases.

Typhus Fever.—The volume of urine is gradually, though not profoundly, diminished up to the third week of this disease. The color is increased up to the crisis, after which it becomes normal, and during convalescence it is lighter than in health. The reaction of the urine is sharply acid. The urine may remain practically free from deposit, although about the crisis a deposit of urates is frequent. The quantity of uric acid is increased, though less marked, and less uniformly so than urea. The most notable feature of the urine, however, in typhus is the marked reduction in the quantity of chlorides, which in severe cases practically amounts to complete absence or retention. This is not due to diarrhœa, lack of food, or other readily explainable cause, but seems a constant feature of the disease itself.

The urine in typhus is frequently albuminous, perhaps more frequently so than in typhoid, although there is some difference of opinion upon this point. Most are agreed, however, that in the more severe forms of the disease albuminuria is the rule. The quantity of albumin in the urine varies much, but is frequently in large amount in serious cases; appearing usually toward the crisis of the disease, most often on or about the sixteenth day.

DISEASES OF THE LIVER.

Cirrhosis.—The quantity of urine is constantly diminished in cirrhosis of the liver, so constantly indeed that a copious flow of urine may be considered strongly presumptive evidence of the absence of this disease. Diuretics act with difficulty or fail to be effective until the congestion of the liver be modified by mercurials or purgatives, and it is in such cases that calomel acts as a diuretic. The color of the urine is markedly increased, being dark, red, brown, and even blackish. The acidity of the urine is increased, and, unlike in pyrexial states, the acidity rapidly intensifies after the urine is voided. The dark coloration of the urine is due to the presence of bile-pigments in the urine. So constant, indeed, is the association of bile-pigment in the urine in this disease that it may serve to distinguish ascites of hepatic origin from that of peritoneal effusion, especially in non-febrile forms of the latter. The excessive bile-pigmentation of the urine in cirrhosis of the liver receives its most plausible explanation in the facts of long detention of the blood in the liver, where the red corpuscles are subjected to prolonged metamorphosis.

The solids of the urine vary widely in quantity in cirrhosis of the liver, chiefly in consequence of the great variability of

Glucose + Levulose increased
NH^4 + amino Acids greatly increased
see
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the appetite and digestion, the stomach being subject to more or less disturbance in these cases through implication with the cirrhotic process. With a normal appetite and digestion the quantity of urea is subject to little change. On the other hand, the quantity of uric acid is pretty uniformly above normal, and often very considerably so. The chlorides are somewhat deficient; most so in cases attended by ascites, the ascitic fluid becoming heavily charged with sodium chloride. Deposits of amorphous urates and calcium-oxalate crystals are common. Albuminuria is rare, save in cases depending upon valvular lesions of the heart. The urinary sediment, as a rule, does not contain renal casts and other evidences of nephritis, save in very exceptional cases, mostly due to cardiac disease.

Jaundice.—As a rule, the volume of urine suffers some reduction in jaundice, although it is often quite up to the normal range. The quantity of urea, as a rule, is diminished; the uric acid is increased; the sulphates are not especially altered in quantity; hippuric acid is usually absent; the urine is always highly acid, the acidity rapidly intensifying after the urine is voided. The color of the urine depends upon the presence of bile-pigments, and varies from saffron-yellow to dark greenish brown or sometimes porter color. The bile-pigments are sometimes present in the urine in very large quantity, as well as the bile-acids. Benzoic acid fails to be eliminated by the urine as hippuric acid, contrary to conditions of health. In marked cases sugar sometimes appears in the urine, and this may be regarded as an unfavorable indication.

The chief value of examinations of the urine in jaundice is to establish the diagnosis at an early period. Our present tests for bile-pigments enable us to ascertain when the disease is coming on, as these products appear in the urine very early. The presence or absence of bile-elements, as well as leucin and tyrosin, in doubtful cases assists in distinguishing between obstructive and non-obstructive jaundice.

Acute Yellow Atrophy.—This somewhat rare and rapidly-fatal disease is attended by marked icterus and by extensive destruction of the hepatic cells. The urine is strongly acid in this lesion, and contains both bile-pigments and the bile-acids. The quantity of the urine is much diminished, though not suppressed, and the color is usually very dark brown. The urine usually contains leucin or tyrosin or both, the former nearly always, and sometimes in very large quantity. The quantity of urea is greatly lessened and sometimes nearly absent; uric acid and phosphates are usually reduced in quantity. The urine sometimes contains albumin and casts, although with no great constancy, and when casts are present they often appear yellow from staining with bile-pigment.

ARTICULAR DISEASES.

Acute Rheumatism.—In rheumatic fever the general features of the urine are typically those of pyrexia. The quantity of urine is diminished; the specific gravity is increased, as is also the color; the reaction is sharply acid, and on cooling the urine deposits sediments of deeply-colored urates. The quantity of solids is increased, but chiefly that of urea. The increase of urea usually reaches from 150 to 250 grains above the normal daily range. The quantity of uric acid is somewhat increased, though to a much less extent than urea. A copious precipitate of urates usually occurs at or shortly following the crisis of the disease, and as convalescence becomes established this tendency subsides. The chlorides are subject to a considerable reduction in quantity, though not to so extreme a degree as in pneumonia. The return of chlorides is comparatively early, usually as soon as the temperature declines to 100° F. and the joint-swellings begin to subside. The sulphates are increased in quantity to a marked degree, usually reaching double the normal range. In acute rheumatism and pneumonia the blood contains a marked excess of fibrin, and these two diseases furnish the most marked examples of increase of sulphates in the urine of all acute fevers. The quantity of phosphates in the urine is not materially altered in acute rheumatism.

Albumin often appears in the urine in small amount, but it is usually transient. Exceptionally it occurs in marked quantity, attended by nephritis. In such cases, morphological elements are found in the urinary sediment characteristic of nephritis. The kidneys, however, are less frequently, as well as less profoundly, affected than in pneumonia.

Acute Gout.—Before the attack of gout, or, in other words, between the paroxysms, the urine is more or less deficient in solids, especially those of uric acid, urea, extractives, and phosphates. In the case of uric acid the reduction is greatest immediately before the attack, when it may, indeed, be totally absent. The same thing occasionally occurs in chronic gout during the formation of tophaceous deposits.

During the attack the volume of urine diminishes more or less markedly. Exceptions to this rule occur in cases characterized by chronicity. The frequent co-existence of cardiac hypertrophy and early renal cirrhosis in chronic gouty subjects furnishes the key to the solution of the occasional polyuric form of gout, as well as those exceptional cases attended by deficiency of urea in the urine. As a rule, the excretion of urea is not materially altered during the paroxysm of gout. Garrod first pointed out the now well-known fact that the urine is greatly deficient in uric acid in gout; and this applies both to the attack and the intervals between the paroxysms. Sir William Roberts, pursuing the chemistry of the subject further, has shown[1] that the uric acid is retained and precipitated in the tissues in a state of combination as biurate. The urinary pigment, on the whole, is somewhat deficient in gout. Exceptions to this occur in cases attended by pyrexia. The phosphates of the urine are markedly deficient, notably those of sodium, which doubtless goes to make up the tophaceous deposits in the joints. The sulphates are not essentially altered in quantity.

The urine frequently contains albumin, nearly always in minute quantity, and sometimes it is a permanent condition. Casts are often to be seen in the urine, nearly always of the small, narrow, hyaline order. These features are usually the result of accompanying cirrhosis of the kidney, which is very frequent in gout. Crystals of calcium oxalate are frequent features of the urinary sediment. In chronic gout this same deficiency of uric acid occurs throughout, though more intermittently so.

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[1] Croonian Lectures for 1892.

Diseases of the Nervous System.

Epilepsy.—In the intervals between the epileptic seizures observations thus far have failed to establish any changes of a constant character in the urine, although the urea, uric acid, chlorides, and phosphates have been claimed to be diminished. Immediately succeeding the attacks the volume of the urine is often markedly increased, of pale color, of low specific gravity, feebly acid in reaction, and sometimes contains albumin, more rarely sugar. During and immediately succeeding the attacks the urea and phosphates are increased and deposits of urates and uric acid are common.

Hysteria.—Perhaps no physical phenomenon is more widely known than the marked increase and pale, aqueous appearance of the urine during or immediately succeeding an attack of hysteria. The urine resembles precisely that voided after copious libations of water. The color is pale, "watery," the specific gravity is greatly lessened, the acidity is diminished, and the solids are relatively reduced. The quantity of urine voided by hysterical patients is sometimes very large; two or even three pints is not at all uncommon at one passage. It is, perhaps, not generally or widely known that in hysterical states the urine is sometimes totally suppressed. Laycock was the first to point out this fact, and more recently Charcot has called special attention to this matter, and has recorded a case in which no urine whatever was secreted for eleven days. The utmost watchfulness of the patient was ordered, so that deception was not possible. The patient suffered much of the time from vomiting, and the ejections contained urea. No other serious symptoms ensued, and the urine was ultimately re-established spontaneously. The author has observed, in cases of hysteria due to nervous exhaustion, that the volume of urine for twenty-four hours often becomes reduced to 15 ounces or even less, which he attributes to the deficient vascular tension and insufficient supply of nervous force to the kidneys.

Meningitis.—The urine in meningitis is more or less highly concentrated. The specific gravity is accordingly high, but the reaction is weakly acid, sometimes alkaline. The phosphates are greatly in excess, and are readily precipitated in large amount upon boiling the urine. The chlorides are normal or slightly increased. The quantity of urea is uniformly above normal, the increase usually amounting to 25 per cent. or more. The urine usually contains a small quantity of albumin as a transient condition.

DISEASES OF THE RESPIRATORY ORGANS.

Pulmonary Tuberculosis.—The urine is subject to considerable variation in its characters in tuberculosis of the lungs, in consequence of the numerous incidental complicating conditions present,—such as diarrhœa, pyrexial periods, copious diaphoresis or expectoration,—as well as the great variability in the quantity of food taken. As a rule, the volume of urine is somewhat augmented. This is largely due to the increased quantity of water consumed, thirst being more or less constant in consequence of the pyrexia. During attacks of diarrhœa the volume of urine decreases temporarily, often to 30 ounces and sometimes even to 15 ounces. The same decrease precedes a fatal termination of the disease. If the appetite remain good, and the disease be proceeding without marked disturbing features, the urea remains about normal in quantity, perhaps slightly below. During marked hectic the quantity of urea diminishes decidedly, especially just before the rigors; after the rigors it rises rapidly and reaches its highest excretion about an hour before the sweating stage begins. In cases of intestinal irritation accompanied by vomiting, diarrhœa, anorexia, etc., the quantity of urea is subject to sudden and decided decrease. Uric acid suffers little, if any, reduction; in fact, it usually rises above the normal range. The sulphates are little, if any, affected,—perhaps slightly reduced. The excretion of chlorides varies very much, the variation depending chiefly upon the quantity of food taken, the degree of pyrexia, and the degree of elimination by the skin and bowels. The quantity of pigment varies in phthisical urine owing to the disturbing influences of hectic, diarrhœa, and pyrexia. A pink sediment is often seen in phthisical urine, especially during hectic stages, and the precipitated urates often become of a pink or carmine hue. In cases rapidly progressing toward a fatal issue the diazo reaction of Ehrlich is sometimes obtained in the urine. If this reaction be present for any length of time the prognosis may be regarded as unfavorable.

Albumin is often present in the urine of phthisis, the quantity being usually small, except in cases complicated by amyloid kidneys. The milder grades of albuminuria are chiefly due to impaired nutrition of the renal epithelium, though occasionally, perhaps, the result of pyrexia. Renal casts, epithelium, and blood are found in the urine exceptionally, the casts chiefly in cases complicated by renal lesions, of which amyloid disease is the most frequent, and this is usually associated with cases of marked chronicity.

Pneumonia.—The general pyrexial characters of the urine are well marked in pneumonia. The quantity of urine is diminished one-third to one-half. The quantity of urea is increased, as is also uric acid; the greatest increase occurs on the so-called critical days. It is at such times that enormous deposits of amorphous urates are so often observable in pneumonia,—more marked than in other febrile diseases of equal degree of pyrexia. The specific gravity of the urine is increased 1025 to 1035. Pigmentation of the urine is markedly increased, which intensifies the color of the precipitated urates to deep brown, red, or even carmine. The increase of pigment often reaches two or three times the normal range.

The chlorides are invariably greatly diminished or absent during the early stages and commencing hepatization. This deficiency of chlorides continues until convalescence is well established, sometimes for several days after, when they re-appear in great excess, indicating their retention during the active stages of the disease. The absence of chlorides indicates a period of danger in pneumonia. The sulphates are uniformly increased in pneumonia from one-fourth to one-third above the normal range; only exceptionally do cases occur without being attended by this increase. The quantity of phosphates in the urine suffers more or less reduction.

Of the morbid products met with in the urine in pneumonia, albumin is by far the most constant, the average being about 45 per cent. of all cases. Albumin usually appears in the urine at the height of the disease, especially during the stage of consolidation. Its appearance in notable quantity must be looked upon as an unfavorable indication; the death ratio reaches from 45 to 50 per cent. in such cases, while in non-albuminuric pneumonia the death ratio is only about 15 per cent. The fact that albuminuria is so frequent in pneumonia—perhaps as frequent as in any other febrile disease—strongly favors the now generally-accepted view of the infectious nature of the disease, for albuminuria is now known to be one of the most frequent features of infectious fevers. Furthermore, the albuminuria of pneumonia is evidently independent of the intensity or extent of the local pulmonary lesions and of the disturbed function of the lungs, since frequently cases of the most extensive consolidation and urgent dyspnœa are unattended by albuminuria; while, on the other hand, cases of comparatively mild grade are often accompanied by both albuminuria and nephritis. The kidneys are often seriously damaged in pneumonia; the nephritis sometimes remains comparatively latent throughout convalescence, as in scarlatina, to be discovered weeks or months after the pneumonia has subsided, attention being called to the condition through uræmia, dropsy, or some of the usual symptoms of nephritis. From the above considerations, as might be expected, the urine of pneumonia often contains blood, epithelium, casts, and the usual products associated with nephritis. The urine also contains an excess of mucus, which renders the urine unstable; hence, the urine in pneumonia possesses a decided tendency toward alkaline decomposition, and its reaction quickly becomes alkaline upon standing.

Exceptionally pneumonia is attended not only by diminished volume of urine, but also by decrease of the solids, including urea and uric acid. Such cases are almost invariably characterized by delayed convalescence, diarrhœal attacks, and slow recovery. The proportion of solids in the urine is, in fact, one of the most trustworthy guides for prognosis in pneumonia, and cases attended by diminished excretion never proceed so favorably as those in which the solids are excessive.

During convalescence the volume of the urine increases; the quantity of uric acid, urea, and sulphates, previously excessive, now gradually diminish to or below the normal range; while the chlorides, previously held back, now increase considerably above normal, often, in fact, to an extraordinary degree.

Acute Pleurisy.—The urine in pleurisy presents the usual febrile type, though not so pronouncedly as in pneumonia. The volume is reduced; the organic solids are increased, notably during pyrexia. Both urea and uric acid are somewhat excessive. The chlorides, sulphates, and phosphates are but little changed; sometimes there is a reduction in the quantity of chlorides, but not to any marked degree. Albuminuria is uncommon in pleurisy; sometimes it appears in mild form, but it is usually of temporary duration. The urine often contains a very considerable amount of peptone, especially during the stage of resolution, when absorption of large serous effusion is in progress. Pleurisy presents an example of the fact that intense pain often causes but little effect over tissue metamorphosis, since few pyrexial states present so little alterations in urine indicative of tissue waste as does simple pleurisy.

Acute Bronchitis.—The urine in bronchitis varies much in character in different cases. This, indeed, is to be expected, since the grades of the disease are of all degrees, from slight catarrh of the large tubes to disease including nearly all the small tubes of both lungs, with collapse of the air-cells, to the extent of entailing sharp dyspnœa. In the latter case the urine approaches the same characters as those in pneumonia.

In cases of severe diffuse capillary bronchitis accompanied by dyspnœa, there is usually a marked diminution of nearly all the solid constituents of the urine, more so than perhaps in any other disease save cholera. Parkes records the case of a young man who, during two days, voided but 294 cubic centimetres of urine per day, containing only 244 grains of total solids, 176 grains of which were urea, 10.8 grains of sulphates, and no chlorides. There was no albuminuria or symptoms of uræmia, and the urine became gradually established as the patient recovered. Moos has recorded a similar case in a girl who, during the height of the disease, excreted only 9 grammes of urea (139 grains) and 2 grammes of sodium chloride. The conditions favoring the retention of chlorides are those interfering with proper aëration of the blood, and there is reason to believe that when these conditions are extreme the same influence extends to the entire solids of the urine. The urine is occasionally albuminous in bronchitis, but this condition is nearly always transient; implication of the kidneys being rare.

DISEASES OF THE DIGESTIVE SYSTEM.

Under the term "dyspepsia" a number of symptoms are commonly grouped which are often of widely different causation, and many of which are only recently becoming understood, notably some of the forms associated with auto-intoxication. In chronic disorders of the stomach and intestines the urine is often increased in quantity, of pale color, of lowered specific gravity, with a tendency toward alkaline reaction from fixed alkali. In consequence of the alkaline tendency of the urine, there is a proneness to precipitation of the earthy phosphates, and such urine is often turbid from this cause when voided. As a secondary consequence, vesical irritation is a common accompaniment which not infrequently leads to the formation of gravel. The quantity of urea depends upon the digestive power of the stomach. Usually the quantity of urea in the urine is below normal, often markedly so; the quantity of chlorides correspond closely with the amount of food taken.

In disorders of the intestinal tract attended by increased albuminous decomposition the urine is apt to contain large amounts of so-called indican, and this is especially favored by obstinate constipation or obstructive diseases.

In organic diseases of the stomach and intestines, especially if associated with ulcerative changes, the urine often contains notable quantities of peptone. A mild type of albuminuria is sometimes associated with disorders of the stomach, and it is, indeed, remarkable how frequently the so-called functional albuminuria is found associated with disorders of the stomach. In such cases, though the albuminuria is persistent, often extending over periods of years, it is rare to find casts in the urine or other evidences of nephritis. Small quantities of sugar are sometimes found in the urine in dyspeptic conditions. Of the urinary sediments found in digestive disorders, calcium-oxalate crystals and amorphous phosphates are the most common.

APPENDIX.

EXAMINATION OF URINE FOR LIFE-INSURANCE.

The examination of the urine for life-insurance has for its object the determination of the presence or absence of diseases of the urinary organs which tend to abridge the normal expectancy of life. As a special field of urinary diagnosis, this has grown to very extensive proportions in nearly all civilized countries, and, since the interests involved are so important and wide-spread, the subject is well deserving of special consideration.

The questions involved in the examination of the urine for purposes of life-insurance often call for a high order of skill and judgment for their accurate determination, and experience has demonstrated that the adoption of systematic methods of conducting the examination not only simplifies the subject, but also renders the conclusions reached more trustworthy. It has, therefore, become the custom with many insurance associations to furnish certain rules as a guide in conducting examinations of the urine, which are intended to cover the more important points of information desired. Notwithstanding these precautions, life-insurance associations still find a very large percentage of their unprofitable risks arise through diseases of the kidneys which have escaped detection. It is with a view of contributing to the avoidance of such losses, on the one hand, and, on the other, of securing to applicants the privileges of life-insurance to which they may be fairly entitled, that the following suggestions are presented as a guide for medical examiners.

A due regard for the interests of his company, as well as for his own reputation, should prompt the medical examiner to personally ascertain that the urine about to be examined has been voided by the applicant. Substitutions of healthy urine by unhealthy applicants are matters of undoubted facts in the history of insurance circles, and, though fortunately of infrequent occurrence, the examiner should be on his guard against such possible source of imposition. The applicant should be directed to retain his urine for, say, two or three hours before presenting himself for examination; and upon his arrival he should be given a clean glass vessel and requested to void therein his urine, which is always preferably done in the presence of the medical examiner; but if this be impracticable, the temperature of the urine should be immediately noted in order to guard against possible imposition. This method also secures a perfectly fresh sample of urine —always a matter of prime importance—and, moreover, voided at a time most desirable for the purpose, viz., after food and exercise; for it should not be forgotten that the urine voided on rising in the morning (which it has become somewhat the custom to furnish for these purposes) is the least likely to contain either albumin or sugar, when these are present in minute quantities.

If the examination of the urine be unsatisfactory, or if there be reason to believe that the sample examined be not a fair average, it will be advisable to have the whole twenty-four hours' product of the kidneys *collected*, *mixed*, and *measured*, and a sample of this mixture examined, and compared with a freshly-voided sample of the urine.

PHYSICAL EXAMINATION OF THE URINE.

Having secured a perfectly-fresh sample of the applicant's urine, it should be allowed to stand until it cools down to a temperature of about 75° or 78° F., and careful observation made of its appearance and physical characters. If the color be very light (watery), it suggests diminished specific gravity, possibly hydruria,—diabetes insipidus. Should the color be of decided greenish tint, the possible presence of sugar is suggested: should the color be unduly increased,—reddish,—excess of urates or the presence of blood is inferred; in the first case suggesting rheumatic or gouty conditions; in the latter, calculi or some organic renal or vesical lesion. The transparency or opacity of the urine should be carefully noted: if cloudy, add a few drops of acetic or other acid to a sample in a test-tube, and if the urine become perfectly cleared thereby the earthy phosphates in suspension was the cause of the opacity, their suspension being due to diminished acidity of the urine, and it suggests some such condition as fasting, dyspepsia, or general debility. If the opacity of the urine fail to yield to the action of an acid, gently warm the upper layers of the urine by holding the test-tube over a spirit-flame, and if it now clear the opacity was due to suspension of the amorphous urates, the significance of which has already been stated. If, however, the urine still remain cloudy after treating it with both heat and acid, the opacity is due to the presence of pus bacteria or cellular elements, and the necessity of microscopical examination is suggested for diagnostic purposes.

The specific gravity of the urine should next be observed by the aid of a good instrument,—preferably a Squibb's specific gravity instrument (urinometer),—and the range should be near 1020. If the specific gravity, however, be above 1025, it suggests the possible presence of sugar; if below 1018, it is suspicious of the presence of albumin, and should lead to further investigations in these special directions.

The chemical reaction of the urine should next be ascertained by means of litmus-paper. If found to be very sharply acid, as indicated by intense reddening of blue litmus, the possibility of the presence of sugar is suggested, since the urine is more sharply acid when it contains sugar than in most other conditions. Should the urine be frankly alkaline in reaction, as indicated by decided blue coloration of red litmus-paper, the paper should be dried in order to ascertain if the alkalinity of the urine be due to fixed or volatile alkali. If the red color return upon drying, after having turned blue in contact with the freshly-voided urine, ammonium is present or volatile alkali, and this suggests the presence of some chronic inflammatory condition of the lower urinary tract, most likely the bladder. If, on the other hand, the blue color remain permanent upon drying the paper, the urine is alkaline from fixed alkali, and indicates unusual alkalescence of the blood, which may suggest fasting, dyspepsia, or vegetarian habits of eating.

A careful survey of the physical characters of the urine, as just indicated, will often lead further investigation in certain directions, and also lend confirmation to the points brought out by further investigations of the urine. But even though all the physical characters of the urine be found perfectly normal, the urine cannot be positively asserted to be healthy until search has been made at least for sugar and albumin, since either or both of these may exceptionally be present in small amounts without their presence being indicated by a physical inspection of the urine.

CHEMICAL EXAMINATION.

The most simple chemical examination of the urine for purposes of life-insurance should, at least, include a search for sugar and albumin and a quantitative estimation of the urea.

Albumin.—If the urine contain albumin in large or even medium quantity, it will be made apparent by almost any of the ordinary tests for albumin in use. When, however, the urine contains but minute quantities of albumin, the case is altogether different, and the greatest care is absolutely necessary not only to be able, in all cases, to positively identify it, but also to interpret its true significance. To the search for small quantities of albumin in the urine, therefore, the following considerations are intended chiefly to apply:—

The urine frequently contains such foreign substances as peptone (deutero-proteose), vegetable alkaloids, and oleoresins, besides an excess of such normal constituents as mucin and urates. With some reagents for albumin the substances just named give reactions almost precisely like those due to small quantities of albumin in the urine. It is of the utmost importance to be able to readily and positively distinguish the presence of albumin in the urine from the substances just named. Nothing is really more simple than to make such a distinction with due regard to chemical laws; for it consists simply in employing methods that give reactions with albumin while they do not give similar reactions with the substances named. This, however, has not been the method hitherto uniformly recommended, but, rather, it has often been advised to surround old and radically faulty methods (some of which have long outlived their usefulness for this purpose) by corrections and precautions which render them often complex, if not confusing.

The medical examiner is advised to discard the use of heat as a test for minute quantities of albumin in the urine. The author has ceased to employ it for such purposes for over ten years, save in the form laid down as No. 2, and only thus for confirmative purposes, for he has long since become acquainted with more trustworthy and ready methods. The following method of applying test No. 4, described in the text (page 74), will be found to be simple, rapid, and trustworthy. Into the bottom of an ordinary test-tube pour from 15 to 30 drops of acetic acid, and to this add about double that amount of aqueous solution of potassium ferrocyanide (1 to 20). Next, add sufficient urine to half or two-thirds fill the test-tube. Close the top of the tube with the thumb and invert the test-tube three or four times to insure thorough mingling of the reagents with the urine, and then stand the tube in a good light. In from half a minute to two minutes, if albumin be present even in minute traces it will come plainly into view in the form of a milk-like turbidity. This method will bring albumin to view with great certainty, while it will not bring similarly to view any of those substances named, which often produce albumin-like precipitates with many other tests.

Since Heller's nitric-acid test has hitherto been somewhat popular in insurance circles, it may be proper to here state the additional reasons for the author's preference for the ferrocyanic test.

The nitric-acid method of Heller is a ready and excellent test in the presence of considerable amounts of albumin in the urine. When mere traces of albumin are present, however, it requires from twenty minutes to half an hour to bring it to light with certainty. In addition to this the reactions of this test with mucin, oleoresins, urates, etc., require corrections and precautions which demand skillful manipulation and interpretation to reach trustworthy results; and, therefore, the interests both of the company and the applicant are best served by the use of the simpler and more trustworthy methods. The quantity of albumin in the urine is most rapidly determined by the centrifugal method described on page 83.[1]

Significance of Albuminuria.—Having positively identified the presence of albumin in the urine, in all cases its true significance should be next traced.

As a rule, minute quantities of albumin in the urine are less likely to be the result of serious disease of the kidneys in young people than when met with in people beyond middle age. A very considerable percentage of such cases in the young belong to that class which has been termed *physiological* or *functional albuminuria*, terms which are meant to indicate that the kidneys are not structurally damaged. In such cases, in addition to the fact that the subjects are mostly young, the urine presents certain fairly uniform features, viz.: the specific gravity of the urine is usually increased to 1025 or above; albumin is often absent from the urine on rising in the morning, but appears plainly after exercise, food, or mental excitement; the urine is free from renal casts and significant morphological elements; and the quantity of urea in the urine remains normal. While many such cases continue for years without any marked changes either in the urine or in the general health of these subjects, yet a certain proportion of them ultimately develop into serious nephritis. The fact that we possess no positive data by means of which we can with certainty distinguish the special cases of this class which will ultimately terminate unfavorably from those which will pursue a favorable course, and, furthermore, since nephritis is more liable to arise from slighter causes in these cases than ordinarily, it cannot be affirmed that these cases are safe risks. It has been suggested by some authorities that these cases might be accepted for a limited endowment insurance of, say, five or ten years, but the safer course for the company would be delay for sufficient time to determine the ultimate course of the case. These questions, however, will be determined by the medical director at the home office, to whom all the facts and particulars of such cases should be carefully reported.

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[1] It has been shown (pages 83 and 84) that the unit of measurement of Esbach's albuminometer-tubes, as ordinarily supplied by the dealers, is too large (1 gramme) for accurate measurement of small amounts of albumin in the urine. Messrs. Eimer & Amend, of 205 and 211 Third Avenue, New York, now manufacture and supply these albuminometers, the first three grammes of the reading being graduated in tenths of a gramme, which obviates the above-named objection. Moreover, these tubes are specially adapted for use with the author's electric centrifuge, so that those who prefer Esbach's quantitative method to the author's may carry out the test in two or three minutes.

Traces of albumin are sometimes observable in the urine of perfectly healthy people, the reaction being due to dissolved morphological elements, and such is most frequently observed in women the subjects of leucorrhœa, or in men with slight bladder irritation. If such urine be permitted to stand in a conical glass for a few hours, or if it be submitted to the centrifugal apparatus, a deposit, mostly of epithelium and mucous corpuscles, becomes plainly visible to the naked eye. The nucleo-albumin of these structures becoming dissolved out, often renders the urine sufficiently albuminous to cause slight reaction in testing if the quantity of epithelium, etc., be abundant. It may be necessary, therefore, in the cases of women, to direct a vaginal douche to be used previous to voiding the urine for examination, while in other cases it may be necessary to quell the vesical irritation by medical treatment before passing opinion upon the true state of the urine.

Minute quantities of albumin are often observed in the urine of men at and beyond middle age, who not only appear perfectly healthy, but who have, as a matter of fact, enjoyed the most typical robust health all their lives. *Among this class will be found the largest number of those cases which have always proved so unprofitable to life-insurance associations, through concealed or overlooked disease of the kidneys.*

Two features in this class of cases stand out so prominently that they are well calculated to mislead the medical examiner, viz., (*a*) the robust general condition of seemingly perfect health of the applicant and (*b*) the minute (often doubtful without careful testing) traces of albumin in the urine often accompanying these cases. These facts teach us two highly-important lessons which the medical examiner would do well to remember: 1. That a healthy appearance or healthy personal record of the subject carries less weight, in reaching conclusions as to certain pathological conditions of the kidneys, than in any other disease. 2. That the presence of traces of albumin in the urine, however minute, are often the index of irretrievably-damaged kidneys.

Chronic interstitial nephritis, or so-called chronic Bright's disease, to which the foregoing facts especially apply, is nearly always the outgrowth and sequel to robust life, the kidneys being the first organs to fail under the stress of long-continued functional activity in eliminating the waste-products, which are always excessive in people of large appetites and ample nourishment. These cases present the following typical features: The subjects are, as a rule, over 40 years of age; usual history of robust health; appetite always good, often heavy; and the food has consisted largely of meat and highly-nitrogenous products. These people usually rise regularly at night—once, twice, or oftener—to void their urine, which, to all appearance, is normal and free from sediment. The urine, however, is usually of lowered specific gravity,—1018 to 1014,—more or less deficient in urea, and contains a small amount—often mere traces—of albumin. Microscopical examination merely shows the presence of a few small, perfectly hyaline casts. The pulse is always full, hard, and unresisting to the finger,—almost characteristically so; the second sound of the heart is abnormally loud, and in many cases enlargement of the heart is plainly to be observed. If the above-named points be kept in view, the medical examiner will have no difficulty in recognizing this dangerous class of risks.

Sugar.—In searching for sugar in the urine, it is of prime importance to have on hand some trustworthy and stable test that may be depended upon when required. Fehling's solution has been much depended upon, but its well-known instability greatly detracts from its usefulness for the purposes under consideration. Fehling's solution will not keep, for reasons explained (page 109), and its preparation requires some time and pains. A better test, more simple in preparation and sufficiently stable that it may be kept on hand for months without impairment of its qualities for testing, is that devised by Professor Haines (page 103). This test, if properly manipulated, will yield as trustworthy results as it is possible for any copper test to give.

In searching for sugar with Haines's test, 1 drachm of the test-solution, in an ordinary test-tube, should be raised to the boiling-point over a spirit-lamp, and the suspected urine should be added, drop by drop, until 8 or 10 drops are added, *but not more.* The test should now be boiled for about half a minute, and, if sugar be present, a copious yellow or yellowish-red precipitate will suddenly appear throughout the whole mixture. If no such reaction take place, sugar is absent. The chief feature in the manipulation to be kept in mind is not to add more than the stated limit (8 or 10 drops) of urine. If this be disregarded and the urine be added (as in Fehling's test) to a volume equal to the test-solution, or thereabout, any urine may cause reaction when sugar is absent. This is due to the fact that normal urine contains certain substances (chiefly uric acid, creatinin, etc.) which possess feebly reducing powers over copper tests; and, therefore, if the urine be added in excess the test is liable to respond to these agents.

In exceptional cases the urine may contain an excess of uric acid or other reducing substances just named, or such foreign elements as tannin, carbolic acid, or vegetable alkaloids, which may cause slight reaction with this or any copper test. For the most part, this reaction is usually an imperfect one, the test-solution turning green rather than yellow or red, though exceptionally a frank yellow precipitate may be formed. Such cases, however, in reality are very rare, if the test be manipulated as directed. Should any doubts, however, arise as to the presence of sugar, after thorough cleansing of the test-tube and carefully repeating the test in all particulars, as directed, an appeal may be made to the phenylhydrazin test, as described (page 105), which may be considered conclusive. Having identified the presence of sugar in the urine, its exact quantity may be readily and rapidly determined by the author's method, already described in the text (page 110).

Significance of Sugar in the Urine.—The presence of sugar in the urine, in a general sense, is nowise less serious in its signification than is that of albumin. As in the case of albumin, the tendency has been to look upon small quantities of sugar in the urine as of no grave import; but recently this view of the subject is giving way to a belief that, as a rule, the presence of sugar in the urine, regardless of the quantity, means serious defect, either in the brain or the liver, or in both, and this view will prove the safer one to follow. It is true that in a few conditions, notably in some forms of indigestion, as well as over-ingestion of highly-saccharine or amylaceous foods, small quantities of sugar may appear in the urine in the absence of a diabetic state. On the other hand, genuine diabetes mellitus is often preceded for a time by precisely these symptoms, viz.: the appearance of small quantities of sugar in the urine, often, indeed, intermittent, but always aggravated by indulgence in saccharine or starchy foods. The author is unable to identify the special cases of the former class which subsequently do or do not terminate in diabetes, but he is able to affirm, from observation, that many of these cases of so-called "*digestive glycosuria*" end in fatal diabetes, more especially in young subjects. It has been truthfully said, by an author of wide experience on this subject, that "a man with sugar in his urine is like a house that is undermined; he will surely fall, but no one can predict the precise time that the disaster will occur." It will be safer to accept this assertion as a guide in such cases.

Urea.—An examination of the urine can scarcely be considered complete which does not include an estimate of the quantity of its contained urea. Representing, as it does, by far the greater bulk of the organic output of the kidneys, the quantity of urea in the urine becomes a valuable index of the functional capacity of the kidneys, and, therefore, serious forms of disease of these organs is usually quickly and markedly reflected in the diminished excretion of urea.

The estimation of urea in the urine is now a matter of such simplicity and rapidity that it ranks among the more simple manipulative methods, such as testing for albumin and sugar, and, in reality, requires but little more time. The method best suited for the purposes under consideration is that known as the hypobromite test, which is most readily performed with Dr. Doremus's ureometer. A fresh solution of sodium hypobromite is necessary for testing, as the solution does not keep well. This is best obtained as follows: Have on hand a quarter- or half-pound bottle of bromine, and, after once opened with care, set it aside for use. Next prepare a solution of sodium hydroxid (caustic sodium) by dissolving 3 ounces of caustic sodium (in sticks) in 8 ounces of distilled water, which may also be kept on hand for use. In preparing the solution of sodium hypobromite for testing, pour 10 cubic centimetres of the caustic-sodium solution into a graduated glass, and with the pipette (furnished with the ureometer) take up 1 cubic centimetre of bromine[1] and mix thoroughly with the caustic-sodium solution; next add an equal volume of water, and, after thoroughly mixing until the solution becomes *transparent*, fill the bulb of the ureometer with the solution, and incline the instrument until the hypobromite solution fills the long arm. Next thoroughly cleanse the pipette, and take up 1 cubic centimetre of the urine and slowly discharge it into the hypobromite solution, in such position that the disengaged nitrogen-gas will all ascend the long arm of the instrument, where it is measured. As soon as the urea is all decomposed, as indicated by no further ascending of bubbles, read off the quantity as indicated by the amount of nitrogen-gas marked on the long arm of the instrument. Each number represents the fractions of a gramme of urea per cubic centimetre of urine, of which 0.02 is the normal proportion. If preferred, these ureometers are furnished with a scale indicating the number of grains of urea per ounce of urine instead of grammes per cubic centimetre.[2]

The normal quantity of urea is about 512 grains in twenty-four hours for a man of 145 pounds weight, upon a mixed diet and moderate amount of exercise. This gives an approximate proportion of 10 grains of urea per ounce of urine, the whole quantity of the urine being 50 ounces. It will be necessary to make an allowance of about 25 or 30 per cent. from this standard in order to cover variations caused by differences in weight, age, diet, and exercise. If, therefore, the gross quantity of urea sink below 350 grains (7 grains per ounce), there is reason to apprehend the presence of some organic disease of the kidneys. Should the deficiency be still more marked, the quantity of urea diminishing to 250 or 200 grains (5 grains per ounce), it furnishes strong evidence of diseased kidneys. On the other hand, a normal amount of urea in the urine, coupled with the absence of albumin therefrom, strongly indicates that the kidneys are healthy. Certain it is that no very advanced renal disease can be present under such circumstances.

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[1] Avoid inhaling the strong vapor of the bromine, which is very irritating to the air-passages.

[2] These instruments are furnished by Eimer & Amend, 205 and 211 Third Avenue, New York, at moderate cost.

MICROSCOPICAL EXAMINATION.

A microscopical examination of the urine is often required of the medical examiner in cases of applications for heavy amounts of insurance. In addition to this, in cases in which a chemical examination of the urine has not been conclusive, a microscopical investigation should be made. It is not proposed to here enter into the technique of microscopy, which every one has access to in the numerous works especially devoted to the subject. A few general suggestions in reference to the special subject herein considered may, however, be of use.

The urine for microscopical examination should in all cases be freshly voided, and it is better to have it somewhat concentrated by directing the applicant to abstain from the use of fluids for a few hours previous to voiding the urine for examination. Where practicable, the sediment is preferably obtained by the centrifugal method. Should the centrifugal apparatus not be available, proceed by adding 10 grains of resorcin, chloral hydrate, or salicylic acid to the urine, in a conical glass, to preserve it from change, and, after covering the glass, stand it aside for from twenty-four to forty-eight hours, until the sediment subsides. Then take up from 4 to 6 drops of the sediment, by means of a nipple pipette, from the bottom of the deposit, and place them in a shallow cell; cover the cell with a cover-glass, take up the overflow of urine with the torn edge of a piece of blotting-paper, place the slide under the microscope, and examine deliberately with a one-fourth-inch objective, avoiding too brilliant illumination of the field, since too much light tends to render hyaline casts invisible, as they are feebly refractive. Careful search should be made over at least two slides prepared as above directed, noting the presence and relative number of pus- or blood- corpuscles, but more especially the presence, number, and characters of any renal casts. If no pathological products be found after examination of two slides, the evidence may be considered conclusive in the negative.

PYURIA.

The medical examiner will encounter but little difficulty in detecting the presence of pus in the urine of the applicant if it be present in any notable quantity. Such urine is always more or less cloudy when voided, and the turbidity does not clear up by the addition of an acid or the application of heat; on the contrary, the cloudiness is rather increased by these agents. A sediment, more or less pronounced, quickly settles to the bottom of the vessel, and if the urine be decanted from the sediment and liquor potassæ added to the latter, it thickens into a jelly-like consistence, and becomes ropy and sticky, as will be observed in pouring it from the vessel. Should any doubts arise, however, as to the nature of this deposit, the microscope will readily reveal the presence of characteristic corpuscles, described in the text (page 180).

The significance of pyuria may be very grave; it can scarcely ever be considered trivial, inasmuch as it points to bacterial infection of the urinary tract. In people beyond middle age it is nearly always a serious matter, since in such people the resisting powers of the system against pyogenic germs are much diminished, and consequently the infection under such circumstances is more likely to extend than to subside. Moreover, the causes which most often provoke pyuria in elderly people are of a permanent nature.

On the other hand, pyuria in younger subjects is often the index of tubercular pyelitis, pyonephrosis, etc., which are not only, as a rule, incurable diseases, but often rapidly fatal ones. Pyuria in its least serious signification is the associate of mild forms of cystitis in otherwise healthy subjects, and as such it is usually soon recovered from, in young or even middle-aged subjects, under properly-directed treatment. On the whole, pyuria should be looked upon as more or less serious, and the only safe course to pursue in these cases is to recommend delay of the application for a few weeks until it be determined if the condition be a permanent one.

HÆMATURIA.

Application will scarcely be made for life-insurance if blood be present in the urine in sufficient amount to attract the attention of the applicant. Should such be the case, however, the examiner will not be likely to overlook cases of pronounced hæmaturia, as they will be apparent upon the most superficial inspection of the urine. But the urine may become so highly colored from concentration as to conceal minute quantities of blood; or, again, blood may be present in quantities so minute that it merely lends to the urine a deep shade of normal coloration. Close inspection will usually distinguish the abnormal tint due to blood, and upon standing the distinction will usually be more marked in the sediment. In cases of doubt, however, the microscope will readily detect the presence of the blood, in quantities however minute it may be present.

The examiner should always inquire for a history of attacks of hæmaturia, with the circumstances associated therewith. The appearance of blood in the urine, occurring at irregular intervals, often indicates the presence of gravel, or the beginning of such still more serious diseases as renal tuberculosis and cancer of the kidney. If hæmaturia has appeared, inquiries should be made as to its character, the frequency of the attacks, as well as its extent. Thus, if the blood appeared intimately mingled with the urine, of dark color, and without clots, it may be concluded that its source was renal, and it would be presumptive evidence of the presence of more or less serious disease. On the other hand, if the blood appeared somewhat separate from the urine, of a brighter and more arterial tint, and associated with small clots, it may be concluded that it originated from the lower urinary tract, most likely the bladder, and further inquiry is likely to elicit symptoms of stone, villous growths, early tuberculosis, or even malignant disease. Unless in the early stages of the conditions just named, the accompanying symptoms will be so pronounced that they could scarcely be overlooked. There is a period, however, in the early stages of most of these diseases, in which mild hæmaturia may be almost the only symptom observable; hence the importance of ascertaining its occurrence. It will be a safe rule for the medical examiner to consider a subject in danger of serious disease of the kidneys or bladder who presents a history of hæmaturia, unless five years have passed since the last appearance of such attacks, the urine remaining in the interval in all respects normal.

CALCULI.

An examination of the urinary organs cannot be considered complete without inquiring for any attacks of renal colic or the passage of calculi by the applicant. A number of such attacks may have occurred, and even small calculi may exist and be in process of growth in the kidneys without any evidence thereof being present in the urine.

The passage of renal calculus, however small, is usually attended by symptoms of so marked and characteristic an order that it will be distinctly remembered by the applicant upon interrogation. The sudden onset of pain in the side without any apparent cause; the intense suffering for some hours, in which the pain extends along the course of the ureter, often retracting the testicle on the affected side; frequently accompanied by nausea, vomiting, cold perspiration, and even some degree of collapse, and followed by sudden and complete relief. These form a chain of phenomena so pronounced and distinctive that they are neither likely to be overlooked by the applicant nor misinterpreted by the medical examiner.

A man may have one or more such attacks, and the symptoms may permanently disappear without calculus lodging and developing into calculous disease. Such cases are termed spontaneous recovery; but it is not safe to class cases in this category until at least five years have passed since the last attack, the urine remaining constantly free from pus and blood. Under the latter circumstances it may be concluded that the conditions which favored the formation of calculi have passed away. If, on the other hand, attacks have been frequent, and especially if there have been recent attacks, it may be concluded that the conditions favorable for the development of calculous disease in the urinary tract still continue, and such cases cannot be safely recommended for life-insurance.

From the sum of these considerations the following rules may be formulated, as a concise guide in conducting examinations of the urine and reaching conclusive data as to the condition of the kidneys and urinary organs in life-insurance:—

Rules.

1. Secure a freshly-voided sample of urine for examination, preferably after food and exercise, and be certain that the urine examined has been voided by the applicant.

If the examination result in any doubts as to the true conditions present, procure a sample of a mixture of the whole twenty-four hours' product of the kidneys, and also another freshly-voided sample of the urine; examine both of these separately and compare carefully the results.

2. Carefully observe first the physical characters of the urine, more especially: (*a*) *The appearance.* If cloudy, ascertain the cause, whether due to phosphates, urates, pus, blood, etc. The color, whether light (watery) like hydruria, or greenish (diabetic-like), or normal straw-yellow. (*b*) *The specific gravity.* If 1025 or above, search for sugar. If below 1020 search for albumin, and also ascertain the total amount of urea. (*c*) *The chemical reaction.* If very sharply acid (possibly diabetic, rheumatic, or gouty conditions are present). If alkaline from fixed alkali (probably debility, dyspepsia or fasting, or vegetable diet). If ammoniacal (cystitis is suggested).

3. Examine next for albumin with the ferrocyanic test as directed. Do not ignore the presence of albumin, *however minute the quantity* may be. If in any doubt as to the presence of minute traces, take two perfectly-clean test-tubes half full of the suspected urine. To one apply the ferrocyanic test, but to the other add no reagent whatever. Stand the two side by side in a good light for ten minutes. If they remain alike, albumin is absent; if faint opacity occur in the one with the test, albumin is present.

4. Examine next for sugar with Haines's test as directed.

Boil 1 drachm of this test; add 8 or 10 drops of the urine,—*no more;* boil again half a minute. If sugar be present, a yellow or yellowish-red precipitate will appear. If no such precipitate appear, sugar is absent. If a gray or whitish precipitate occur, it is caused by earthy phosphates, and not sugar. If any doubts arise as to the presence of sugar by the copper test, appeal to the phenylhydrazin test for confirmation.

5. An estimation should next be made of the quantity of urea in the urine with the Doremus ureometer, but especially if the specific gravity of the urine be materially reduced. Should the proportion of urea be 25 per cent. below normal, or lower, estimate the whole excretion of urea for twenty-four hours, and if below 300 grains report the fact to the home office.

6. In cases in which a microscopical examination of the urine is requested by the company, carefully report the following features of the urinary sediment: (*a*) The presence, quantity, and features of pus- or blood- corpuscles, *i.e.*, whether well preserved or partly broken down. (*b*) The presence, number, and characters of any renal casts, especially noting their size, whether clear or granulated, and if any epithelium or blood-corpuscles are seen attached to the casts.

7. Inquire for a history of attacks of renal colic (passage of calculi) or hæmaturia. Report the number and special features of such attacks, especially the severity and length of time they may have continued, and the *date of the last attack.*

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Hexamethyamin in Urine

10 cc Urine in test tube
at 37°C

Sol Phenylhydrazin
HCl [illegible] 100 cc
Phenylhydr .5 gm
azine 100
3 drops —

5% Nitroprusside
Sodium Sol — 3 drops

Sat Sol Na HO a few
drops poured along side
test tube — purple blue Color
changing to dark green — over

Boston Med & Surg Journal
Oct 24 1912

Capillary Constant of
Combe of Lausanne
My bulb with filtered
water gives 50 drops to
empty bulb—

Scheme—

Sp Gr Urine 1.020

Σ = 1.020 – 1000 = 20

No of drops H_2O 50×

" " " ~~Water~~ Urine 55×

Δ – 110 – 100 = 10

$\frac{\Delta}{\Sigma}$ = = .5

Normal constant

.8 – to 1.5 indicate intestinal
decomp

23. **Uric Acid in the Urine.**—Dreyfus thus describes the Hopkins-Folin method of determining uric acid:

(1) A solution of 1 litre volume containing 500 grams of ammonium sulphate; 5 grams of uranium acetate; 60 c.c. of 10 per cent. acetic acid; and distilled water to bring the bulk up to 1 litre. (2) A one-twentieth normal solution of potassium permanganate.

The method of procedure is as follows: Place 300 c.c. of urine in a beaker, add 75 c.c. of the ammonium sulphate reagent, and mix thoroughly. After the precipitate has settled sufficiently (say in about five minutes) filter through a double folded filter. When 250 c.c. of the filtrate has passed through, this volume is divided into two portions of 125 c.c. each, to serve as a duplicate. To each portion add 5 c.c. of concentrated water of ammonia, mix thoroughly and allow to stand over night. The precipitated ammonium urate is then transferred to a filter and washed with a 10 per cent. solution of ammonium sulphate. Then wash the precipitate with about 100 c.c. of water into the same beaker, add 15 c.c.

of concentrated sulphuric acid, and immediately titrate with N/2
solution of potassium permanganate until the first permanent tin
of pink color appears. One c.c. of potassium permanganate sol
tion equals 3.75 milligrammes of uric acid. From this calcula
the amount in twenty-four hours.

A shorter process, but one which is less accurate, consists in t
precipitation of uric acid with ammonium chlorid (30 grams f
each 100 c.c. of urine), allowing it to stand over night, then filt
ing off the ammonium urate, washing with cold saturated so
tion of ammonium chloride, and dissolving in hot water (ab
100 c.c.), containing about 15 c.c. of concentrated sulphuric ac
and titrating as before.

Boston Medical and Surgical Journal.

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3. **Albumoses in Urine.**—Elmer mentions the f
the diseases in which albumosuria occurs most
Multiple myeloma of bones, tuberculosis, especially
croupous pneumonia in the stage of resolution, se
emia, abscess, carcinoma and sarcoma when und
retrograde changes, and the leukemias and Hod
after treatment with Roentgen rays. He recom
lowing test for albumose as being the most p
reagent consists of a 50 per cent. solution of
acid in distilled water. This reagent precipitates
proteids found in the urine, but the albumoses
warming the urine, while albumins, globulins,
that when any or all of the albumin group a
albumoses filtered the warmed urine will sepa
the albumoses be determined by cooling the filtr
be taken to avoid prolonged boiling, for if mu
they may be broken down, one of the products
mose. A very small quantity of albumoses
by dividing the urine after adding the reage
one part while cooling the other and compari
fore a dark surface.

Ammonia in urine - Formalin test

A.M.A. - V 55 - 812 - 131

original papers?

ANSWER.—The indigo test of Penzoldt depends on the transformation of orthonitrobenzaldehyd into indigo blue. A few crystals of orthonitrobenzaldehyd are dissolved in hot water and, after cooling, a little of the fluid to be tested and some sodium hydrate solution are added. If acetone be present the fluid turns yellow, then green, and then blue (indigo formation). If desired, the indigo can be shaken out with chloroform and further tests for its identity made. The test can be applied directly to the urine, and will yield a positive reaction if acetone be present in abundance, but for the detection of small amounts of acetone it is necessary to distill off 30 to 40 c.c. from 250 c.c. of urine, using a cooler. The most of the acetone passes over in the first 10 to 20 c.c. of the distillate, and the test is applied to the distillate. Penzoldt's test is very reliable and free from objection. Many prefer it to Legal's test. Penzoldt's article will be found in the *Deutsches Archiv f. klin. Med.*, vol. xxxiv (1883), p. 132. Recent studies by Ellram and also by von Meickebecke confirm the reliability of the test. Strauss' method for the determination of indican, in a rough way, quantitatively, for clinical purposes, is as follows: Twenty c.c. of urine are mixed with 5 c.c. of a 20 per cent. solution of acetate of lead. Ten c.c. of the filtrate (equal to 8 c.c. urine), are placed in a separating funnel, which is closed below by a glass stopcock and above with a glass stopper; it is graduated to 5, 10, 15, 20 and 25 c.c. To the 10 c.c. of the filtrate are added 10 c.c. of Obermayer's reagent (concentrated hydrochloric acid containing 2 grams of perchlorid of iron per liter) and 5 c.c. chloroform; the tube is shaken gently several times, allowed to stand for some time and shaken again. The chloroform solution is then drawn off, more chloroform placed in the separating funnel, and the process repeated until the chloroform extracts no more color. After this 2 c.c. of the combined chloroform extracts are placed in a test tube of the same size and form as the test tube containing a control solution of indigotin in chloroform (1 mgr. in 1,000 c.cm.). The colored chloroform solution is diluted with pure chloroform until the color is the same as that of the control solution. The quantity of indican present is easily calculated. If x is the amount of chloroform in cubic centimeters used for extraction, and y the amount used for dilution, then $\frac{1}{2}xy$ would give the chloroform value from which the amount of indigo can be calculated, it being remembered that the test solution contains 0.001 gm. of chemically pure indigotin in 1,000 ccm. and that 8 ccm. of urine was used for the reaction. The control test tube of the standard solution should be kept in a dark cupboard. Strauss has published his method in the *Deutsche med. Wochenschrift*, vol. xxix (1902), p. 299. A somewhat similar colorimetric method has been introduced by J. Bouma (*Deutsche med. Wochenschrift*, vol. xxviii, 1902, p. 705). Bouma uses a so-called indicanurometer which consists of eleven test tubes of the same size and thickness arranged in a row. Six of these contain a solution of indigo red (of urinary origin) in chloroform, the strength varying so as to correspond to 5, 10, 15, 20, 30 and 40 mg. of indigo per liter of urine. The tubes are hermetically sealed and serve as control solutions. They must be kept in the dark. To make Bouma's test, 10 ccm. of urine are precipitated with 2 ccm. of lead acetate solution. One places 5.5 ccm. of the filtrate (=5 ccm. urine) in a test tube and adds 10 ccm. of isatin-hydrochloric acid solution (20 mg. purest isatin [Merck] dissolved in 1 liter chemically pure, iron-free, concentrated hydrochloric acid). The tube is heated to boiling for some seconds, then cooled and the contents extracted by shaking with 5 ccm. chloroform. This chloroform extract is compared with the six control solutions and the quantity thus immediately determined. It must be emphasized that these tests give only approximately accurate results, though they are perhaps sufficient for clinical work. More accurate methods, but much more difficult of application, are those of Wang (*Zeitschr. f. physiol. Chemie*, vol. xxv, 1898, p. 406), and of J. Bouma (*Zeitschr. f. physiol. Chemie*, vol. xxxii, 1901, p. 82).

If Indican sol has greenish tint add picric acid to
Indigo sol to correspond with the greenish tint

midge's improved method of examining the urine in suspected cases of pancreatic diseases are as follows: A specimen of the twenty-four hours' urine, or of the mixed morning and evening secretions, is filtered several times through the same filter paper and examined for albumin, sugar, bile, urobilin and indican. A quantitative estimation of the chlorids, phosphates and urea is also made, and the centrifugalized depósit from the urine examined microscopically for calcium oxalate crystals. If the urine is found to be free from sugar and albumin, and of an acid reaction, 1 c.c. of strong hydrochloric acid (specific gravity 1.16) is mixed with 20 c.c. of the clear filtrate, and the mixture gently boiled on the sandbath in a small flask, having a long-stemmed funnel in the neck to act as a condenser. After ten minutes' boiling the flask is well cooled in a stream of water, and the contents made up to 20 c.c. with cold distilled water. The excess of acid present is neutralized by slowly adding 4 grams of lead carbonate. After standing for a few minutes the flask is again cooled in running water and the contents filtered through a well-moistened, close-grained filter-paper until a perfectly clear filtrate is secured. The filtrate is then well shaken with 4 grams of powdered tribasic lead acetate and the resulting precipitate removed by filtration, an absolutely clear filtrate being obtained by repeating the filtration several times if necessary. The large amount of lead in solution is removed either by treatment with a stream of sulphuretted hydrogen or by precipitating the lead as a sulphate. For this purpose the clear filtrate is well shaken with 2 grams of finely-powdered sodium sulphate, the mixture heated to the boiling point, then cooled to as low a temperature as possible in a stream of cold water, and the white precipitate removed by careful filtration; 10 c.c. of the perfectly clear transparent filtrate is made up to 18 c.c. with distilled water and added to 0.8 gram of phenylhydrazin hydrochlorate, 2 grams of powdered sodium acetate and 1 c.c. of 50 per cent. acetic acid contained in a small flask fitted with a funnel condenser. The mixture is boiled on a sandbath for ten minutes, and then filtered hot through a filter paper moistened with hot water into a test-tube provided with a 15 c.c. mark. Should the filtrate fail to reach the mark, it is made up to 15 c.c. with hot distilled water. In well-marked cases of pancreatic inflammation a light yellow, flocculent precipitate should form in a few hours, but it may be necessary to leave the preparation to stand over night before a deposit occurs. Under the microscope the precipitate is seen to consist of long, light yellow, flexible, hair-like crystals, arranged in sheaves which, when irrigated with 33 per cent. sulphuric acid, melt away and disappear in from ten to fifteen seconds after the acid first touches them.

The urine employed for the experiment should be fresh, and not have undergone fermentative changes. If alkaline in reaction it should be made acid with hydrochloric acid before the test is commenced; any glucose that may be present should be removed by fermentation after the urine has been boiled with the acid, and the excess neutralized.

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over

THE FOLIN METHOD FOR ESTIMATING THE QUANTITY OF AMMONIA IN THE URINE.

CHICAGO, June 27, 1908.

To the Editor:—When I saw the above heading over an article by Dr. Buhlig in THE JOURNAL, June 27, I thought: Well, finally, I shall know what Folin's method is. I read the article twice and when I had finished, I knew just as much about the Folin method as I knew before, *i. e.*, practically nothing. Will you give a detailed description of the test? S. K.

ANSWER.—It is to be regretted that an omission was made in the publication of the article by Walter H. Buhlig on "The Folin Methods of Estimating the Quantity of Ammonia in the Urine" in THE JOURNAL, June 27, 1908. Part of the legend was omitted by mistake; it should have appeared as given here. This makes clear the reference to reagents mentioned in the body of the original article by Dr. Buhlig. It might be added that a suction pump is attached to the right hand end of each apparatus, in the Folin apparatus (Fig. 1) to draw air through and to carry the liberated ammonia from bottle B into the standard acid, and in the Shaffer apparatus (Fig. 2) to make a low pressure so that the liberated ammonia will distill over from flask B into the bottles of standard acid.

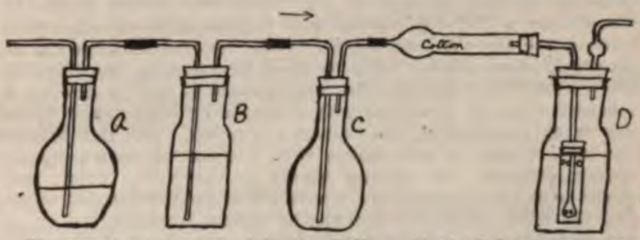

Fig. 1.—Apparatus used in the Folin method of determining the ammonia content of urine, with the addition of an air-filled flask, C: A, dilute H_2SO_4; B, 50 c.c. urine, 20 gm. NaCl, 20 c.c. petroleum, 2 gm. Na_2CO_3, added last; C, air flask; D, 30 c.c. n/5 H_2SO_4 + distilled H_2O.

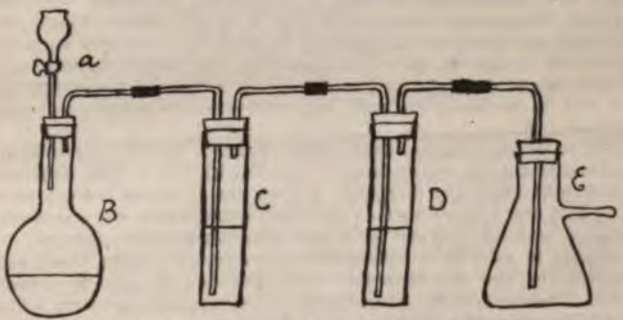

Fig. 2.—Apparatus used in Shaffer's vacuum distillation method: B, 50 c.c. urine, 15-20 gm. NaCl, 50 c.c. methyl alcohol, 1 gm. Na_2CO_3; C, 25-50 c.c. n/10 H_2SO_4; D, small amount n/10 H_2SO_4 + H_2O.

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